

# preparatis gamoyenebis instruqcia P

**pegasisi**®  
PEGASYS®

peginterferoni alfa – 2°

## 1. aRweriloba

### 1.1 Terapiuli/farmakologiuri jgufi:

imunomastimulirebeli agenti/citokini, aTq kodi: L03A B11

### 1.2 dozirebis forma

pegasisi gamoSvebulia saineqciod gamzadebuli Spricebis da ampulebis saxiT

- saineqciod gamzadebuli Sprici Seicavs 180mkg peginterferon alfa-2a-s gaxsnils 0.5 ml saineqcio xsnarSi.

- saineqciod gamzadebuli Sprici Seicavs 135mkg peginterferon alfa-2a-s gaxsnils 0.5 ml saineqcio xsnarSi

- erTjeradad gamoyenebadi 1 ml-iani ampula, Seicavs 180mkg peginterferon alfa-2a-s

- erTjeradad gamoyenebadi 1 ml-iani ampula, Seicavs 135mkg peginterferon alfa-2a-s

### 1.3 Seyvanis forma: kanqveSa ineqcia

### 1.4 steriloba/ radioaqtiuri mdgomareoba: monacemebi ar მოძოვება

### 1.5 თვითობრივ-რაოდენობრივი Semadgenloba

aqtiuri nivTiereba: peginterferon alfa-2a

damxmare nivTierebebi: natriumis qloridi, polisorbati 80, benzilis spirto, natriumis acetato, ZmarmJava, saineqcio wyali

## 2. klinikuri maxasiaTeblebi

### 2.1. Terapiuli Cvenebebi:

**qronikuli B hepatiti:** pegasisi naCvenebia orive formis HBeAg -dadebiTi da HBeAg -uaryofiTi qronikuli B hepatitis samkurnalod cirozian da cirozuli dazianebis gareSe RviZlis kompensirebuli daavadebis მქონე პაციენტებისათვის; ასევე, B hepatitis virusis replikasiis da RviZlis anTebiTi reaქციის შემთხვევაში.

**qronikuli C hepatiti:** pegasisi monoTerapiis saxiT an kopegusTan kombinaciaSi naCvenebia qronikuli C hepatitis samkurnalod cirozian da cirozuli dazianebis gareSe RviZlis kompensirebuli daavadebis მქონე პაციენტებისათვის. ასევე, pegasisi/kopegasisis kombinacia naCvenebia aranamkurnaleb da pegilirebuli an standartuli alfa-interferonis mono- an ribavirinTan kombinirebulი Terapiis mimarT rezistentuli qronikuli C hepatitis samkurnalod. pegasisis efeqturoba dadasturebulia aiv-Tan Tanainfeქციის SemTxvevaSic.

### 2.2 dozireba da miRebis wesi

#### qronikuli B hepatiti

qronikuli B hepatitis HBeAg -dadebiTi da HBeAg -uaryofiTi formebis dros pegasisi naCvenebia 180 mkg/kviraSi doziT 48 kviris ganmavlobaSi. ineqcia tardeba kanqveS muclis an barZayis midamoSi.

#### qronikuli C hepatiti

qronikuli C hepatitis dros rogorc monoTerapiis, ise kopegusTan (ribavirinTan) kombinaciaSi pegasisis rekomendirebuli dozaa 180 mkg/kviraSi. ineqcia tardeba kanqveS muclis an barZayis midamoSi. kopegusis miReba xdeba sakvebTan erTad. pegasisiT monoTerapiis dros mkurnalobis rekomendirebuli xangrZlivobaa 48 kvira. pegasisisa da ribavirinis kombinaciIT mkurnalobisas mkurnalobis xangrZlivoba damokidebulia C hepatitis genotipze:

C hepatitis pirveli genotipis dros mkurnalobis dawyebidan 4 kviraSi gansazRvradi HCV rnm-is SemTxvevaSi rekomendirebulia mkurnaloba 48 kviris ganmavlobaSi. C hepatitis pirveli genotipis SemTxvevaSi mkurnalobis dawyebisas dabali virusuli datvirTviT (< 800,000 IU/ml) an meoTxe genotipis SemTxvevaSi mkurnalobis dawyebidan 4 kviraSi aragansazRvradi HCV rnm-is SemTxvevaSi, rac aragansazRvradi rCeba aseve mkurnalobis dawyebidan 24 kviris Semdeg. mkurnalobis xangrZlivobaa 24 kvira. Tumca mTels populaciaSi mkurnalobis xangrZlivobis Semcireba 24 kviramde zrdis recidivis risks 48 kvirian mkurnalobasTan SedarebiT. aseT pacientebSi gasaTvaliswinebelia kombinirebuli Terapiis amtanoba da fibrozis xarisxi. mkurnalobis xangrZlivobis Semcireba 24 kviramde genotipi 1-is, maRali virusuli datvirTvis (> 800,000 IU/ml) da amasTan, aragansazRvradi HCV rnm-is SemTxvevaSi mkurnalobis dawyeba me-4 da 24 kviraze kidev ufro safrTxiloa, radganac arsebobs mwiri monacemebi, rom aseT pacientebSi mkurnalobis kursis Semokleba uaryofiad moqmedebs myari virusuli pasuxis miRwevaze (ix. cxrili 1 da Tavi 3.1.2.-klinikuri efeqturobis kvlevebi). 2 da 3 genotipis dros meoTxe kviraze aragansazRvradi HCV rnm-is SemTxvevaSi sawyisi virusuli datvirTvis miuxedavad mkurnalobis xangrZlivoba Seadgens 24 kviras. mkurnalobis 16 kviriani kursi SeiZleba sakmarisi iyos 2 da 3 genotipis, dabali sawyisi virusuli datvirTvis da meoTxe kviraze aragansazRvradi HCV rnm-is mqone pacientebisaTvis. mkurnalobis 16 kviriani kursi 24 kvirian kursTan SedarebiT xasiaTdeba recidivis ufro maRali sixSiriT (ix. Tavi 3.1.2.-klinikuri efeqturobis kvlevebi). mkurnalobis kursis Semcirebis gadawyvetisas gasaTvaliswinebelia kombinirebuli Terapiis amtanoba da fibrozis xarisxi. mkurnalobis xangrZlivobis Semcireba 16 kviramde 2 da 3 genotipis, maRali sawyisi virusuli datvirTvis da meoTxe kviraze aragansazRvradi HCV rnm-is mqone pacientebSi safrTxiloa, radgan mkurnalobis xangrZlivobis Semcirebam SeiZleba gazardos recidivis riski (ix. Tavi 3.1.2.-klinikuri efeqturobis kvlevebi). HCV 5 da 6 genotipis mqone pacientebis Sesaxeb monacemebi SezRudulia; amitom rekomendirebulia mxolod 1000-1200mg ribaviriniT mkurnaloba

cxrili 1. C hepatitis kombinaciuri Terapiis dozirebis rekomendaciebi

genotipi	pegasisis doza	kopegusis doza	xangrZlivoba
genotipi 1 . dabali sawyisi virusuli datvirTva swrafi viruuli pasuxi*	180mkg	<75kg – 1000mg >75kg – 1200mg	24 an 48 kvira
genotipi 1. maRali sawyisi virusuli datvirTva. swrafi virusuli pasuxi*	180mkg	<<75kg – 1000mg >75kg – 1200mg	48 kvira
genotipi 4. swrafi virusuli pasuxi*	180mkg	<75kg – 1000mg >75kg – 1200mg	24 an 48 kvira
genotipi 1 an 4. swrafi virusuli pasuxis gareSe*	180mkg	<75kg – 1000mg >75kg – 1200mg	48 kvira
genotipi 2,3 . dabali sawyisi virususli datvirTva. swrafi virusuli pasuxi**	180mkg	800mg	16 an 24 kvira
genotipi 2,3 . maRali sawyisi virususli datvirTva swrafi virusuli pasuxi**	180mkg	800mg	24 kvira

genotipi 2,3 . swrafi virusuli pasuxi**	180mkg	800mg	24 kvira
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\*swrafi virusuli pasuxi= sisxISI C hepatitis virusis rnm- ar aRmoCnda mkurnalobis dawyebidan 4 da 24 kviraze

\*\*swrafi virusuli pasuxi= sisxISI aragansazRvradi HCV rnm-is Sefaseba mkurnalobis dawyebidan 4 kviraze

dabali virusuli pasuxi=  $\leq 800,000$  IU/ml

maRali virusuli pasuxi=  $> 800,000$  IU/ml

### **mkurnalobis mimarT rezistentuli qronikuli C hepatiti**

am jgufis pacientebSi rekomendirebulia kombinirebuli Terapia pegasisiT 180 mkg/kviraSi + kopegusT (ribavirini). pegasisis ineqcia tardeba kanqveS muclis an barZayis midamoSi. kopegusis miReba xdeba sakvebTan erTad. 75 kg-de pacientebSi kopegusi iniSneba 1000 mg doziT, 75 kg-ze meti wonis pacientebSi 1200 mg doziT. 1 da 4 genotipis SemTxvevaSi mkurnalobis rekomendirebuli xangrZlivobaa 72 kvira, xolo 2 da 3 genotipis SemTxvevaSi - 48 kvira.

### **aiv + C hepatitis virusis koinfeqcia**

rekomendirebulia pegasisi 180 mkg kviraSi erTxel kanqveSa ineqciis saxiT monoTerapia an 800 mg kopegusTan kombinaciaSi 48 kviris ganmavlobaSi virusis genotipis miuxedavad. aiv pacientebSi 800 mg-ze maRali doziT kopegusis miRebisas misi efeqturobisa da usafTxoebis kvlevebi ar Catarebula.

### ***mkurnalobis prognozi C hepatitis aranamkurnaleb, axladdiagnostirebuli SemTxvevebSi***

mkurnalobaze pasuxis winaswar gansazRvra (adreuli virusuli pasuxi) xdeba mkurnalobis me-12 kviraze. Tu moxda virusis raodenobis Semcireba 2-logariTmiT an metiT an vlindeba aragansazRvradi HCV rnm, savaraudod mkurnalobis bolos miiRweva stabiluri virusuli pasuxi (cxrili 2).

### **cxrili 2. mkurnalobis prognozi me-12 kviraze adreuli virusuli pasuxis mixedviT sxvadasxva genotipis virusis dros**

genotipi	uaryofiTi efeqti			dadebiTi efeqti		
	aramopasuxe me-12 kviraze	stabiluri pasuxi ar miiRwa	adreuli prognozireba	mopasuxe me12 kviraze	stabiluri pasuxi miiRwa	adreuli prognozireba
1 (n=569)	102	97	55% (97/102)	467	271	58% (271/467)
2, 3 (n=96)	3	3	100% (3/3)	93	81	87% (81/93)

myari virusuli pasuxis uaryofiTi prognozi pegasisiT monoTerapiis SemTxvevaSi Seadgens 98%-s. aiv+ C hepatitis virusis koinfeqciis dros pegasisis monoTerapiis da kopegusTan kombinirebis SemTxvevaSi uaryofiTi prognozis sidide Sesabamisad 100% da 98%-ia. dadebiTi prediqtuli maCvenebeli 45% da 70% aRiniSneba Sesabamisad 1 da 2/3 genotipebis mqone pacientTa kombinirebuli mkurnalobisas.

### ***mkurnalobis prognozi Catarebuli mkurnalobis mimarT rezistentuli C hepatitis SemTxvevebSi***

Catarebuli mkurnalobis mimarT rezistentuli C hepatitis SemTxvevebSi 72 kviriani mkurnalobisas gankurnebis saukeTeso prediqtoria virusis supresia 12 kviraze (HCV RNA  $< 50$  IU/ml). virusis supresiis uaryofiTi prognozuli maCvenebeli 12 kviraze aris 96% (324/339), dadebiTi ki 57% (57/100).

#### **2.2.1 dozireba gansakuTrebul SemTxvevebSi**

*pegasisis dozis modifikacia*

zogadi nawili: dozis modifikacia saWiro xdeba saSualo da mZime gverdiTi efeqtebis gamovlenis SemTxvevaSi (klinikuri an laboratoriuli). preparatis doza mcirdeba 135mkg-mde. zog SemTxvevaSi dozis Semcireba saWiro xdeba 90mkg an 45mkg-iT. dozis Semdgomi momateba sawyis dozamde ganixileba gverdiTi movlenebis alagebis Semdeg (ix, Tavi 2.4gansakuTrebuli miTiTebebi da 2.6.arasasurveli gevrdiTi efeqtebi da 3.8).

hematologia: dozis Semcireba rekomendebulia Tu neutrofilebis raodenoba (ANC) naklebia 750 ujredi/mm<sup>3</sup> -ze, xolo Tu neutrofilebis raodenobam daiklo 500ujredi/mm<sup>3</sup> - mde, mkurnaloba unda Sewydes, sanam maTi raodenoba ar miaRwevs 1000 ujredi/mm<sup>3</sup>-s. mkurnaloba unda daiwyos pegasis 90mkg doziT, aucileblad neutrofilebis raodenobis kontrolis qveS.

aseve aucilebelia dozis Semcireba 90 mkg-mde, Tu Trombocitebis raodenoba naklebia 50000/mm<sup>3</sup>-ze. Terapia unda Sewydes Trombocitebis raodenobis 25000/mm<sup>3</sup>-mde Semcirebis SemTxvevaSi.

RviZlis funqciebi: qronikuli hepatitisTv is damaxasiaTebelia RviZlis funqciebis cvlilebebi. amave dros, rogorc yvela alfa interferoniT mkurnalobis fonze, pegasisiT mkurnalobis drosac aRiniSneba alt-s donis momateba sisxlSi. alt-s progresuli matebis dros C hepatitiT daavadebulebSi Tavdapirvelad doza unda Semcirdes 135mkg-mde. Tu alt-s done matulobs miuxedavad dozis Semcirebisa, savaraudoa bilirubinis donis matebac da RviZlis dekompensirebuli dazianeba, aseT dros saWiroa mkurnalobis Sewyveta (Tavi 2.4 gansakuTrebuli miTiTebebi).

B hepatitis SemTxvevaSi alt-s done zogjer 10-jer aRemateba normul zeda zRvars. Aalt-s donis momatebisas rekomendirebulia RviZlis funqciebis ufro xSiri kontroli. pegasis dozis Semcirebis an mkurnalobis Sewyvets SemTxvevaSi transaminazebis donis daregulirebis Semdeg SesaZlebelia mkurnalobis ganaxleba da Semcirebuli dozis gazrda. (Tavi 2.4 gansakuTrebuli miTiTebebi).

#### kopegusis dozireba kombinirebuli Terapiis dros.

mkurnalobasTan dakavSirebuli anemiis marTvis mizniT kopegusis doza aseve unda Semcirdes 600mg-mde (200mg diliT da 400 mg saRamos) A Semdeg pacientebSi:

- pacientebi gul-sisxlZarRvTa paTologiis gareSe hemoglobinis <10g/dl da >8.5g/dl-mde SemcirebiT.
- pacientebi stabiluri kardiovaskuluri daavadebiT, hemoglobinis >2g/dl-mde SemcirebiT mkurnalobis 4 kviris ganmavlibaSi.

kopegusiT mkurnaloba unda Sewydes Semdegi garemoebebis dros:

- Tu patients kardio-vaskuluri daavadebis gareSe, aReniSneba hemoglobinis Semcireba <8.5g/dl-mde;
- Tu patients stabiluri kardiovaskuluri daavadebis fonze, aReniSneba hemoglobinis Semcireba <12g/dl-mde 4 kviris manZilze dozis Semcirebis miuxedavad;

Tu kopegusis miReba SeCerebulia laboratoriuli maCveneblebis an klinikuri gamovlinebebis gamo, misi miReba uda ganaxldes dabali doziT 600 mg-iT dReSi da gaizardos TandaTanobiT 800 mg-mde dReSi eqimis rekomendaciis gaTvaliswinebiT. mkurnalobis kursis ganmavlobaSi ar aris rekomendebuli kopegusis maqsimaluri dozis (1000mg an 1200mg-s) gamoyeneba.

kopegusis autanlobis SemTxvevaSi, mkurnaloba unda gagrZeldes pegasisiT monoTerapiis saxiT.

dozirebis instruqciebi specialur populaciaSi ix. qveTavebSi 2.5.3, 2.5.4, 2.5.5 da 2.5.6

### **2.3 ukuCvenebebi:**

pegasisi ukunaCvenebia im pacientebSi, romelTac aReniSnebaT hipermgrZnobeloba alfa interferonebis, E.Coli-is warmoebulebis, polieTilenglikolis an sxva komponentebis mimarT. pegasisi ukunaCvenebia:

- autoimunuri hepatitis mqone pacientebSi.

- dekompensirebuli cirozis mqone pacientebSi.
- dekompensirebuli cirozis dros
- axalSobilebSi da 3 wlamde asakis bavSvebSi.
- pegasisi/ribavirinis kombinirebuli Terapia ukunaCvenebia orsul qalebSi
- pegasisiT mkurnalobis dawyebe ukunaCvenebia qulaTa sistemiT Sefasebisas 6 qulaze metis SemTxvevaSi, Tu es qula miRebuli ar aris atazanavirisa da indinaviris mier gamowveuli hiperbilirubinemiT.  
rekomendebulia kopegusis instruqciis gacnoba, pegasisis kopegusTan kombinaciaSi daniSvnis SemTxvevaSi.

## 2.4 gansakuTrebuli miTiTebebi

### 2.4.1 zogadi miTiTebebi

pegasisiT mkurnaloba, rogorc mono- aseve kombinirebuli Terapiis saxiT unda Catardes kvalificiuri eqimis meTvalyureobis qveS.

laboratoriuli normebis Sesamowmeblad. ixileT ribavirinis instruqcia

pegasisiT an pegasis/ribaviriniT kombinirebul mkurnalobas Tan axlavs neutrofilebis da leukocitebis raodenobis Semicreba, xSirad am cvlilebebs adgili aqvs mkurnalobis me-2 kviris bolos. klinikur kvlebebSi sisxlis elementebis raodenobis Semicreba me-4, me-8 kviraze Zalian iSviaTia. Ddozis koreqcia rekomendebulia, rodesac neutrofilebis raodenoba mcirdeba  $<750$ ujredi/mm<sup>3</sup> - mde. (ix. 2.2 dozireba da miRebis wesi). im pacientebSi, romelTac aReniSnebaT neutrofilebis ricxvis Semicreba  $500$ ujredi/mm<sup>3</sup>-ze qvemoT, saWiroa mkurnalobis droebiT Sewyveta, sanam maTi raodenoba ar aiwevs  $1000$ ujredi/mm<sup>3</sup>-mde. klinikur kvlebebSi pegasisiT an pagasis/kopegusiT kombinirebuli mkurnalobisas, neutrofilebis raodenobis Semicreba Seqcevadia dozis modifikaciis an droebiTi Sewyvetis pirobebSi.

pegasisiT an pegasis/ribaviriniT kombinirebul mkurnalobaa xSirad aseve axlavs Trombocotebis raodenobis Semicreba. aRniSnuli maCvenebeli ubrundeba sawyis normalur dones mkurnalobis Semdgom periodSi (ix.2.6.gverdiTi efeqtebi). dozis Semicreba rekomendebulia Tu Trombocitebis done Seadgens  $<50000$ /mm<sup>3</sup>, xolo mkurnalobis Sewyveta - Tu maTi raodenoba  $25000$ /mm<sup>3</sup>-ze dabilia. (ix. 2.2 dozireba da miRebis wesi)

*anemia* (hemoglobini  $<10$ g/l) aReniSneboda kvlevaSi CarTul pacientTa 13%-s, romlebsac utardebodaT pegasisisa da ribavirinis (1000mg an 1200mg doziT) kombinirebuli Terapiis kursi 48 kviris ganmavlobaSi da im pacientebis 3%-s, romlebic Rebulobdnen pegasis/ribavirins doziT 800mg 24 kviris ganmavlobaSi (ix. Tavi 2.6.1.1 laboratoriuili cvlilebebi-hemoglobini da hematokriti). hemoglobinis maqsimaluri daqveiTebe aRiniSneba ribaviriniT mkurnalobis me-4 kviris bolos. rekomendebulia ribaviriniT mkurnalobis Sewyveta mkurnalobis procesSi gul-sisxlZarRvTa sistemis muSaobis gauaresebis SemTxvevaSi, ixileT, ribavirinis instruqcia. (ix. 2.2 dozireba da miRebis wesi). gTxovT aseve, gaecanoT, kopegusis sainformacio furcels pegasisisa da kopegusis kombinaciis gamoyeneba mkurnalobis mimarT rezistentul pacientebSi, romelTac mkurnaloba SeuwydaT hematologiuri darRvevebis gamo Seswavlili ar aris, amitom mkurnalobis dawyebamde kargad unda iyos Sefasebuli mkurnalobis sargebloba da riski.

rekomendebulia mkurnalobis procesSi tardebodes sisxlis rutinuli gamokvlebebi. pegasisiT monoTerapia an pegasis/kopegusiT kombinirebuli Terapia sifrTxiliT unda daeniSnoT pacientebis, romelTa neutrofilebis sawyisi raodenoba  $<1500$ ujredi/mm<sup>3</sup> - ze, Trombocitebis sawyisi raodenoba  $<90000$ /mm<sup>3</sup> - ze da sawyisi hemoglobini  $<12$ g/dl- ze. (ix. 2.2 dozireba da miRebis wesi).

sxva interferonebis msgavsad pegasisi melosupresorul preparatebTan erTad Zalian didi sifrTxiliT gamoyeneba. ribavirinis da azaTioprinis erTad miRebisas mkurnalobis 3-dan me-7 kviramde periodSi vlindeba pancitopenia da Zvlis tvinis supresia. hepatitis sawinaaRmdego antivirusuli preparatis moxsnidan 4-6 kviraSi zemoTaRwerili cvlilebebi ukuganviTradeba. ix.2.4.4

RviZlisa da sxva transplantantebis arsebobisas pegasisisa da kopegusis efeqturoba da usafrTxoeba Seswavlili ar aris. sxva interferonebis moqmedebis msgavsad, pegasisiT da pegasisi+kopegusiT mkurnalobisas dafiqsirda transplantantis mocilebis reaqciebi.

#### *infeqciebi*

vinaidan temperaturuli reaqcia dakavSirebulia gripismagvar simptomebTan, romlebic asocirdeba interferoniT mkurnalobasTan, saWiroa gamoiricxos temperaturuli reaqciis sxva mizezebi, gansakuTrebiT pacientebSi, romelTac aReniSnebaT neitropenia. alfa interferoniT mkurnalobisas SeiZleba gamovlindes seriozuli infeqciebi (baqteriuli, virusuli an fungaluri). aseT SemTxvevaSi saWiroa dauyovnebliv daiwyos infeqciis sawinaaRmdego Terapia da daisvas ZiriTadi mkurnalobis gagrZeleba-Sewyvetis sakiTxi.

#### *autoimunuri daavadebebi*

autoimunuri daavadebebis gamwvaveba SeiZleba aRiniSnebodes alfa interferoniT mkurnalobis dros. Aamitom, sifrTxiliT unda moxdes pegasisis da ribaviriniT mkurnalobis dawyeba autoimunuri daavadebis mqone pacientebSi.

alfa interferonebis gamoyenebisas aRiniSneboda fsoriazis gamwvaveba. am dros unda ganixilebodes pegasisiT da ribaviriniT mkurnalobis gagrZelebis an Sewyvetis SesaZleblobebi.

#### *endokrinuli sistema*

sxva interferonebis msgavsad, pegasis/ribavirinis kombinaciam SeiZleba gaamwvavos hipoTireoidizmi an hiperTireoidizmi. mkurnalobis Sewyvetis sakiTxi dgeba, rodesac ver xerxdeba Tireoiduli cvlilebebis mkurnaloba-marTva. Ggarda amisa, interferonebiT mkurnalobis procesSi SeiZleba dafiqsirdes hiperglikemia da hipoglikemia . Tu ver xerxdeba am simptomebis medikamentozuri kontroli, ar unda daviwyoT pegasisiT mkurnaloba, rogorc mono-, aseve kombinirebuli Tarepiis saxiT. Tu es simptomebi gaCnda mkurnalobis procesSi da ver xerxdeba maTi medikamentozuri marTva, rekomendebulia pegasisiT an pegasis/ribaviriniT mkurnalobis Sewyveta.

#### *neirofsiqiatriuli movlenebi*

mZime fsiqiatriuli gverdiTi movlenebi warmoadgenen rogorc sxva interferonebis, aseve pegasisiT an pagasisis/ribaviriniT mkurnalobis gverdiT movlenebs. depresia, suiciduri fiqrebi, an mcdelobebi SeiZleba gaCndes mkurnalobis procesSi damoukideblad imisa, aReniSneboda Tu ara adre patients fsiqonevrologiuri darRvevebi. pegasisiT, rogorc mono-, aseve kombinirebuli Terapiis dawyeba safrTxiloa fsiqiuri aSlilobis mqone pacientebSi. mkurnalobis procesSi saWiroa msgavsi simptomebis kontroli da marTva. eqimi valdebulia msgavsi gverdiTi movlenebis Sesaxeb gafrTxilos patienti da daarigos, rom msgavsi simptomebis gaCenisTanave acnobos eqims. zog SemTxvevebSi SesaZloa saWiro gaxdes mkurnalobis Sewyvetac. (ix. Tavi 2.6 gverdiTi efeqtebi). pediatriul pacientebSi pegasisis daniSvnisas saWiroa gansakuTrebuli sifrTxilis gamoCena da mudmivi monitoringi depresiis simptomebze, gansakuTrebiT im pacientebSi, romelTac anamnezSi hqondaT an aqvT Tanmxlebi fsiqiatriuli darRvevebi.

#### *ofTalmologiuri movlenebi*

interferonebiT mkurnalobam maT Soris pegasisiT an pegasis/ribaviriniT, SesaZloa gamoiwvios seriozuli ofTalmologiuri darRvevebi, mxedvelobis mniSvnelovan daqveiTebamdec. mkurnalobis dawyebis win aucilebelia patients Cautardes sruli ofTalmologiuri gamokvleva. Tu patients anamnezSi aReniSneba ofTalmologiuri darRvevebi mkurnalobis procesSi aucilebelia maTi perioduli kontroli. mkurnalobis procesSi gamovlenili simptomebi patientma unda acnobos eqims, romelic gadawyvets mkurnalobis gagrZelebis sakiTxs.

#### *gul-sisxlZarRvTa sistema*

vinaidan kardialur movlenebs amwvavebs mkurnalobis dros ribaviriniT gamoweveuli anemia, im pacientebS romelTac bolo 6 Tvis ganmavlobaSi anamnezSi aReniSnebaT kardialuri paTologia ar unda daeniSnoT ribavirini. mkurnalobis dawyebamde saWiroa ekg-s gadaReba. Tu interferoniT mkurnalobis Sedegad garTulda gul-sisxlZarRvTa paTologia dgeba mkurnalobis droebiT an srul Sewyvetis sakiTxi (ix. Tavi 2.2 dozireba da miRebis wesi. gaecanT aseev ribavirinis sainformacio furcels.)

#### *hipermgrZnobeloba*

alfa interferoniT mkurnalobisas SeiZleba aRiniSnebodes hipermgrZnobelobis reaqsiebi (mag. urtikaria, angioedema, bronqokonstriqcia, anafilaqsia). Tu msgavsi simptomebi gaCnda mkurnalobis procesSi, saswrafod unda Sewydes mkurnaloba da Catardes alergiis sawinaaRmdego RonisZiebebi. gardamavali gamonayari ar saWiroebs mkurnalobis Sewyvetas.

#### *respiratoruli sistema*

alfa interferonebiT mkurnalobisas SeiZleba gaCndes gverdiTi movlenebi sasunTqi sistemis mxriv, maT Soris: dispnoe, infiltratebi, pnevmonia da pnevmoniti. auxsneli genezis infiltratebis gamovlenis an filtvebis funqciis gauaresebis SemTxvevaSi rekomendebulia mkurnalobis Sewyveta.,

#### *RviZlis funqciebi*

pacientebisaTvis, romelTac pegasisiT an pegasisi/kopegusiT mkurnalobis procesSi ganuviTardaT RviZlis funqciis uecari dekompensacia, rekomendebulia mkurnalobis Sewyveta.

C hepatiti: iseve rogorc sxva alfa interferonebiT mkurnalobisas, pegasisiT an pagasisi/kopegusis Terapiuli kursis ganmavlobaSi SeiZleba aRiniSnebodes alt-s momateba normis zeda zRvramde miuxedavad virusologiuri pasuxisa. Tu alt-s mateba grZeldeba dozis Semcirebis miuxedavad, rasac Tan sdevs bilirubinis momatebac, saWiroa xdeba mkurnalobis Sewyveta (ix. Tavi 2.2 dozireba da miRebis wesi).

B hepatiti: C hepatitisagan gansxvavebiT, B hepatitis mkurnalobisas mosalodnelia daavadebis gamwvaveba, rac xasiaTdeba alt-s donis mniSvnelovani matebiT. klinikuri kvlevebis mixedviT, pegasisiT B hepatitis mkurnalobisas transaminazebis matebas Tan axlavs RviZlis funqciis msubuqi darRveva dekompensaciis niSnebis gareSe. SemTxvevaTa naxevarSi transaminazebis maCvenebelis zeda zRvarTan SedarebiT 10 jer matebisas, saWiroa pegasisis miRebis Sewyveta; danarCeni sxva preparetebiT mkurnaloba ki unda gagrZeldes. pegasisiT B hepatitis mkurnalobisas rekomendirebulia RviZlis funqciis mkacri kontroli.

#### *aiv+C hepatitis koinfeqcia*

aiv+C hepatitis koinfeqciis dros cirozian pacientebSi pegasisisa da ribavirinis kombinaciasTan erTad maRalaqturma antiretrovirusulma Terapiam - HAART SeiZleba gazardos RviZlis dekompensaciis riski. amitom, aseT SemTxvevaSi, saWiroa RviZlis dekompensaciis niSnebis, maT Soris ascitis, encefalopaTiis, varikozuli venebidan sisxldenis, RviZlis sinTezuri funqciis daqveitebis Sefaseba –mag. Child-Pugh  $\geq 7$  qula. qulaTa jami SeiZleba Seicvalos mkurnalobasTan dakavSirebuli parametrebis cvlilebiT-mag. hiperbilirubinemiaTa da hipalbuminemiiT da, ar aris aucilebeli dakavSirebuli iyos RviZlis dekompensaciasTan. RviZlis dekompensaciis gamovlenis SemTxvevaSi saswrafod unda Sewydes mkurnaloba.

#### *zrda da ganviTareba (pediatriuli pacientebi)*

pegasisis da ribavirinis kombinirebuli Terapiis Sedegad pediatriul pacientebSi SeiniSna wonaSi da simaRleSi CamorCena sawyis maCvenebelTan SedarebiT da metad SesamCnevi iyo 48-kviriani mkurnalobis Semdeg. wonisa da simaRlis asakis Sesabamisi z-maCvenebeli iseve, rogorc wonisa da simaRlis populaciuri normis procentuli maCvenebeli, mkurnalobis

ganmavlobaSi Semcirda. umetes SemTxvevaSi mkurnalobis Semdeg 2 wliani dakvirvebis dasrulebisas zrdis normis (wonis da simaRlis) procentuli maCveneblebi daubruna sawyis (asakis Sesabamisi saSualo wonis sawyisi procentuli maCveneblebi iyo 64% da mkurnalobis dasrulebidan 2 wlis Semdeg 60%; asakis Sesabamisi saSualo simaRlis sawyisi procentuli maCveneblebi iyo 54% da mkurnalobis dasrulebidan 2 wlis Semdeg 56%). mkurnalobis dasrulebisas pacientebis 43%-s aReniSna wonis maCveneblis 15%-iT da metiT Semcireba, 25%-s simaRlis maCveneblis 15%-iT da metiT Semcireba zrdis normebTan SedarebiT. mkurnalobis dasrulebidan 2 wlis Semdeg, SemTxveveTa 16%-Si sawyis procentul maCvenebeTan SedarebiT SeiniSneboda wonis 15%-iT da meti erTeuliT Semcireba, da 11%-Si simaRlis sawyis procentul maCvenebeTan SedarebiT simaRlis 15%-iT da meti erTeuliT Semcireba.

#### **2.4.2 zegavlana manqanis tarebaze**

pacientebisaTvis, romlebsac aReniSnebaT Zilianoba, daRliloba an sxva msgavsi simptomebi, mkurnalobis procesSi dauSvebelia manqanis marTva.

#### **2.4.3 laboratoriuili gamokvleva**

mkurnalobis dawyebis win saWiroa hematologiuri da bioqimiuri laboratoriuili testebis Catareba. mkurnalobis procesSi hematologiuri testebis Catareba saWiroa 2- 4 kviraSi erTxel, xolo bioqimiuri testebis - 4 kviraSi erTxel. damatebiTi laboratoriuili testebis Catareba SeiZleba saWiro gaxdes mkurnalobis procesSi.

pegasisiT da pegasis/kopegusiT Catarebul kvlevebSi CarTvis kriteriumebad miRebuli iyo Semdegi laboratoriuili maCveneblebi:

- Trombocitebi  $>90000/\text{mm}^3$ .
- neutrofilebis absoluturi raodenoba (ANC)  $>1500/\text{mm}^3$ ;
- farisebri jirkvlis hormonebis TSH da T4-is normaluri done an farisebri jirkvlis adeqvaturad kompensirebuli funqcia;
- aiv+C hepatitis virusis ko-infeqcia:  $\text{CD}_{4+} \geq 200/\mu\text{l}$  an  $\text{CD}_{4+} \geq 100/\mu\text{l}$  -  $<200/\mu\text{l}$  aiv-1 rnm  $<5000$  kopia/ml amplikor rnm-1 monitoringis testis versia 1.5 gamoyenebiT (Amplikor HIV-1 Monitor Test, v 1.5)

#### **2.4.4 urTierTqmedeba sxva preparebTan da sxva saxis urTierTqmedeba**

C hepatitis pegasisisa da kopegusis kombinaciiT mkurnalobisas pegasisa da ribavirins Soris farmakokinetikuri urTierTqmedeba ar gamovlenila.

Aaseve, ar aris gamovlenili B hepatitis pegasisisa da lamivudiniT mkurnalobisas lamivudinis gavlena pegasisis farmakokinetikur Tvisebebe. pegasisi 180 mkg/kviraSi doziT gamoyenebisas 4 kviris ganmavlobaSi janmrTel mamakacebSi ar axdenda gavlenas torbutamidis (CYP 2C9, mefenitoinis (CYP 2C19), debriszoqinis (CYP 2D6) da dafsonis (CYP 3A4) farmakokinetikaze. pegasisi citoqrom P-450 fermentis inhibitoria da zrdis Teofilinis AUC-s 25%-iT. Teofilinis AUC –s aseTive cvlileba xdeba standartuli alfa-interferoniT mkurnalobisas.

alfa-interferonebi ainhibireben RviZlis mikrosomul ferments citoqrom P-450-s. pegasisis an pegasisis/ribavirinis kombinirebul kursTan paralelurad Teofilinis miRebisas rekomendirebulia Teofilinis koncentraciis monitoringi sisxlis SratSi da, saWiroebis SemTxvevaSi, Teofilinis dozis Secvla.

klinikur kvlevaSi, sadac monawileobda C hepaitiT daavadebuli 24 pacienti, romlebic imyofebodnen meTadonis CanacvlebiT mkurnalobaze saSualo doziT 95mg(30-150 mg) da mkurnalobdnen pegasisiT 180 mkg/kviraSi sisxlSi, aReniSnaT meTadonis 10-15%-iT maRali koncentracia sawyis donesTan SedarebiT. am monacemebis klinikuri mniSvneloba ar aris cnobili, Tumca aseT SemTxvevebSi saWiroa pacientebis monitoringi meTadoniT intoqsikaciis Tavidan asacileblad.



12 kvirian klinikur kvlevaSi, romliTac ganisazRvreboda ribavirinis moqmedeba zogierTi nukleotidis transkriptazas Seqcevadi inhibitoris (lamivudini, zidovudini, stavudini) ujedSida fosforilirebaze, CarTuli iyo 47 pacienti aiv+C hepatitis virusis koinfeqciiT. nukleotidebis Seqcevadi transkriptazas inhibitorebi ar axdenen gavlenas ribavirinis eqspoziciaze. ribavirinisa da didanozinis erTad miReba ar SeiZleba didanozinisa da misi aqtiuri metabolitebis dideoqsiazenozinis, 5'-trifosfatis eqspoziciis gazrdis gamo.

ribavirinis gamoyenebisas gamovlinda RviZlis ukmrissobis (letaluri gamosavliT), periferiuli neiropaTiis, pankreatitis, simpomuri hiperlaqtatemis/laqtazuri acidozis SemTxvevebi.

kompania „roSis” mier Catarebuli kvlevebis garda arsebobs, aseve, klinikuri kvleva, sadac pegilirebuli alfa 2a interferonis-180 mkg/kviraSi da telbivuridiT mkurnalobisas aRiniSna neiropaTiis ganviTarebis riskis gazrda. am Sedegis meqanizmi ucnobia. neiropaTiis aseTive maRali riski ar gamoiricxeba sxva standartuli da pegilirebuli interferonebis gamoyenebisas. ar aris dazustebuli pegilirebuli an standatuli interferonis upiratesoba telbivuridTan kombinaciaSi samkurnalod.

*azaTioprini:* ribavirinma inozinmonofosfatis dehidrogenazaze inhibitoruli moqmedebis gziT SeiZleba Seaferxos azaTioprinis metabolizmi da 6-meTilTiinozin monofosfatis (6-MTIMP) akumulacia, romelsac axasiaTebis mielotoqsiuri moqmdeba azaTiopriniT namkurnaleb pacientebSi. calkeul SemTxvevebSi, rodesac rivbavirinisa da azaTioprinis kombinaciis sargebloba risks aRemateba, SesaZlebelia am kombinaciis gamoyeneba, Tumca rekomendebulia hematologiuri maCveneblebis kontroli da, saWiroebis SemTxvevaSi, mkurnalobis Sewyveta. (ix. qveTavi 2.4.1 zogadi miTiTebebi)

## **2.5. gamoyeneba specialur populaciaSi**

### **2.5.1. orsuloba**

dauSvebelia pegasisis gamoyeneba orsulebSi. pegasisis moqmedeba reproduqciis unarze qalebSi Seswavlili ar aris. sxva alfa interferonebis msgavsad pegasisis miRebisas maimunebSi aRiniSna menstrualuri ciklis gaxangrZliveba, 17-beta-estradiolisa da progesteronis pikuri koncentraciebis miRwevis Seferxeba. preparatis miRebis Sewyvetic Semdeg aRdga normaluri menstrualuri cikli. pegasisis moqmedeba mamakacebis populaciaSi reproduqciis unarze ar aris Seswavlili. mamr rezus maimunebSi alfa – 2a interferonis  $25 \times 10^6$  IU/kg/dReSi miRebisas reproduqciuli darRvevebi ar gamovlenila. ar arisESeswavlili, aseve, pegasisis teratogenuli efeqtebi. alfa – 2a interferoni sarwmunod zrdis bunebrivi abortebis risks maimunebSi. Mmiuxedavad imisa, rom alfa-2 a interferoniT mkurnalobisas orsuli maimunebis STamomavlebSi teratogenuli efeqtebi ar gamovlenila, pegasisis miRebisas mainc rekomendirebulia kontraceptivebis gamoyeneba.

### *pegasisis gamoyeneba ribavirinTan kombinaciaSi*

ribavirins gaaCnia teratogenuli da embriogenuli moqmedeba, amitom ribaviriniT mkurnaloba winaaRmdegnaCvenebia orsulebsa da orsulebis partniorebSi. ribaviriniT mkurnalobisas reproduqciuli unaris mqone qalebma da maTma partniorebma mkurnalobisas da mkurnalobis dasrulebidan 6 Tvis ganmavlobaSi unda gamoiyenon efeqturi kontracepciuli saSualeba 2 saxeoba. pegasisis ribavirinTan kombinaciaSi gamoyenebisas ix. kopegusis (rivabirinis) gamoyenebis instrucia.

### **2.5.2 laqtaciis periodi**

ar aris dadgenili, xvdeba Tu ara pegasisi/kopegusi dedis rZeSi. yovel SemTxvevaSi, arasasurveლი reaqciebis Tavidan asacileblad unda Sewydes misi miReba laqtaciis periodSi sargeblianoba/riskis gaTvaliswinebiT.

### **2.5.3 gamoyeneba pediatriaSi**

pegasisis efeqturoba da usafrTxoeba ar aris Seswavlili 18 wlamde asakis bavSvebSi. aRsaniSnavia, rom pegasisi saineqcio xsnari Seicavs benzil-alkohols. aRwerilia Warbi benzil-alkoholis zemoqmedebiT gamowveuli axalSobilTa sikvdilobis iSviaTi SemTxvevebi.

dauSvebelia pegasisis gamoyeneba axalSobilebsa da bavSvebSi. (ix. Tavi 2.3 winaaRmdegCvenebebi)

#### 2.5.4 xandazmulis pacientebi

klinikuri kvlevebiT dadgenilia, rom ar aris saWiro specialuri dozireba xandazmul pacientebSi

#### 2.5.5 Tirkmlis ukmarisoba

Tirkmlis ukmarisobis terminaluri stadiis dros rekomendirebulia pegasisis 135 mkg/kviraSi sawyisi dozis gamoyeneba(ix. qveTavi 3.2.5. farmakokinetika gansakuTrebil SemTxvevebSi). Tirkmlis funqciis darRvevis dros, darRvevis xarisxisa da sawyisi dozirebis miuxedavad, aucilebelia pacientebis mkacri monitoringi da gverdiTi efeqtebis gamovlenisas dozis Semcireba. ribavirinis gamoyenebisas ix. aseve kopegusis gamoyenebis instruqcia

#### 2.5.6 RviZlis funqciis darRveva

kompensirebuli cirozis mqone pacientebSi (mag. Child Pugh A), pegasisis gamoyeneba uasafTxoa. dekompensirebuli cirozis (mag. Child Pugh B/C an sisxldena varikozulad gaganirebuli venebidan), SemTxvevaSi pegasisis usafTxoeba Seswavlili ar aris (ix.2.3 winaaRmdegCvenebebi)

Child-Pugh klasifikaciiT pacientebi iyofa “msubuq”, “zomier” da “mZime” jgufebad, rac Seesabameba 5-6, 7-9 da 10-15 qulas Sesabamisad.

Sefaseba	dazianevis xarisxi	qula
encefalopaTia	ararseboba	1
	1-2 xarisxi	2
	3-4* xarisxi	3
asciti	ararseboba	1
	msubuqi	2
	zomieri	3
S-bilirubini (mg/dl) SI erTeuli= miumoli/l	<2	1
	2-3	2
	>3	3
	<34	1
	34-51	2
	>51	3
S-albumini(g/dl)	>3.5	1
	3.5-2.8	2
	<2.8	3
INR	<1.7	1
	1.7-2.3	2
	>2.3	3

\* qulebiT Sefaseba xdeba Trey, Burns da Saunders mixedviT (1966).

#### 2.6.arasasurveili gverdiTi efeqtebi

pegasisiT an pegasisi/ribaviriniT mkurnalobisas mosalodnelia alfa-interferonebisatvis damaxasiaTebeli gverdiTi efeqtebis ganviTareba.

##### 2.6.1. klinikuri kvlevebi

pegasisisa da pegasisi/ribavirinis, alfa-interferonis da alfa interferoni/ribavirinis jgufebSi yvelaze xSirad gamovlenili gverdiTi efeqtebi erTnairi sixSiriTa da simZimiT vlindeba. pegasisiTa da pegasisi/ribaviriniT mkurnalobisas yvelaze xSirad gamovlenili gverdiTi efeqtebi msubuqi an saSualo simZimisaa da ar saWiroebs preparatis dozis cvlilebas an mkurnalobis Sewyvetas.

#### qronikuli B hepatiti

klinikur kvlevebSi 48 kviriani mkurnalobisas da mkurnaobis dasrulebidan 24 kviris ganmavlobaSi dakvirvebis periodSi qronikuli **B** da **C** hepatitebis SemTxvevaSi pegasisis usafrTxoebis profili erTaniri iyo, Tumca gamovlenili gverdiTi efeqtebis sixSire SesamCnevad naklebi iyo qronikuli **B** hepatitis dros. (ix. cxrili 3). gverdiTi efeqtebi pegasisiT mkurnalobisas gamovlinda 88%-Si, lamivudiniT mkurnalobisas -53%-Si, seriozuli gverdiTi efeqtebi ki gamovlinda pegasisis jgufis 6%-Si da lamivudinis jgufis 4%-Si.

mkurnalobis Sewyveta gverdiTi efeqtebisa da laboratoriuili cvlilebebis ganviTarebis gamo saWiro gaxda pegasisiT namkurnalebi pacientebis 5%-Si, lamivudinis jgufSi ki 1%-ze naklebSi. pacientebSi cirozis diagnoziT preparetebis moxsnis saWiroebis sixSire iseTive iyo, rogorc Cveulebriv populaciaSi. pegasisze lamivudinis damateba ar cvlida pegasisis usafrTxoebis profils.

### **qronikuli C hepatiti**

48 kviriani Terapiuli kursis ganmavlobaSi pegasisis monoTerapiis SemTxvevaSi gverdiTi efeqtebis gamovlenis sixSire Seadgenda 9%-s da pegasisi/kopegusi 1000-1200 mg-is kombinaciuri Terapiis SemTxvevaSi ki 13%-s. mkurnalobis Sewyveta gverdiTi efeqtebisa da laboratoriuili cvlilebebis ganviTarebis gamo saWiro gaxda 1% da 3%-Si Sesabamisad. pacientebSi cirozis diagnoziT preparetebis moxsnis saWiroebis sixSire iseTive iyo, rogorc Cveulebriv populaciaSi. pegasisi+kopegusi 1000-1200 mg-is kombinaciis dros mkurnalobis xangrZlivobis 24 kviramde Semcirebam an kopegusis dozis Semcirebam 1000-1200 mg-dan 800 mg-de seriozuli gverdiTi efeqtebi Seamcira 11%-dan 3%-de, maSin roca, mkurnalobis Sewyvetis aucileblobam moiklo 13%-dan 5%-de da kopegusis dozis Semcireba aRiniSna 39% dan 19%-de.

### **pegilirebuli interferon alfa2b-s mimarT rezistentuli qronikuli C hepatiti**

pegilirebuli interferon alfa2b rezistentul pacientebSi 72 kviriani mkurnalobis kursis dros mkurnalobis Sewyveta gverdiTi efeqtebisa da laboratoriuili cvlilebebis ganviTarebis gamo saWiro gaxda pegasisis jgufis 12%-Si da kopegusis jgufis 13%-Si, 48 kviriani mkurnalobis kursis dros ki 6% da 7%-Si Sesabamisad. cirozian pacientebSi, 72 kviriani mkurnalobis kursis dros preparatis miRebis Sewyvetis aucilebloba (13% - 15% pegasisisa da kopegusis jgufebSi) ufro maRali iyo 48 kviriani mkurnalobis jgufTan SedarebiT- 6% -7%- Sesabamisad.. kvlevis dasawyisSive gamoiricxa pacientTa jgufi, romelTac Catarebuli mkurnalobis Sedegad aReniSnaT hematologiuri darRvevebi.

meore kvlevaSi, sadac CarTulni iyvnen pegilirebuli interferon alfa2b-s mimarT rezistentuli pacientebi fibrozis an cirozis Tanaarsebobisas (iSakis SkaliT 3-6 qula) da Trombocitebis ricxviT  $>50,000/\text{mm}^3$ , amasTan, mkurnaloba grZeldeboda 48 kviris ganmavlobaSi, pirveli 20 kviraSi gamovlinda Semdegi laboratoriuili cvlilebebi: hemoglobin $<10 \text{ g/dl}$ -26.3%, neitrofilebi  $<750/\text{mm}^3$  -30%, Trombocitebi  $<50,000/\text{mm}^3$  13%-Si, (ix. 2.4)

### **aiv+C hepatitis virusis koinfeqcia**

aiv+C hepatitis virusis koinfeqciis dros klinikuri gverdiTi efeqtebi pegasisis monoTerapiisa da pegasisi/kopegusis jgufebSi ar gansxvavdeboda **C** hepatitis virusis monoinfeqciis jgufebSi gamovlenili gverdiTi efeqtebisagan.

48 kviriani NR15961kvlevaSi, CarTuli pacientebisaTvis (N = 51)  $\text{CD4}<200/\mu\text{l-iT}$ , mkurnalobis dros gamovlenili gverdiTi efeqtebisa da laboratoriuili cvlilebebis ganviTarebis gamo mkurnalobis Sewyveta pegasisis jgufSi saWiro gaxda 16%-Si, pegasisi+800 mg kopegusis jgufSi-15%, aqedan laboratoriuili cvlilebebis gamo 4% - 3%-Si Sesabamisad. aiv+C hepatitis virusis koinfeqciis dros kombinirebuli Terapiis jgufSi pegasisis dozis Semcireba saWiro gaxda 39%-Si, kopegusis dozis Semcireba ki 37%-Si. seriozuli gverdiTi efeqtebi gamovlinda 21% da 17%-Si pegasisis monoTerapiis da pegasisi/kopegusis jgufSi Sesabamisad. pegasisiT mkurnaloba asocirebuli iyo  $\text{CD4+}$  absoluturi ricxvis SemcirebasTan  $\text{CD4+}$  ujredebis procentobis Semcirebis gareSe. mkurnalobis dasrulebis Semdeg dakvirvebis periodSi  $\text{CD4+}$  ujredebis ricxvi daubruna sawyis mniSvnelobas. dakvirvebis periodSi pegasisis uaryofiTi gavlena aiv viremiazee ar gamovlenila.

cxrilSi 3 naCvenebia gverdiTi efeqtebi, romlebic vlindeboda pegasisiT an pegasisi+ ribavirinis an interferon alfa 2b+ribavirinis jgufebSi 10%-ze maRali sixSiriT

**cxrili 3. gverdiTi efeqtebi (10%-ze maRali sixSiriT gamovlenili  
sxvadasxva jgufebSi)**

	B hepatiti	C hepatiti				aiv+ hepatiti C	peg- interferon alfa2b mimarT rezisten-tuli hepatiti C
	pegasisi 180 µg 48 kvisis ganm. (WV16240 + WV16241)	pegasisi 180 µg 48 kvira (NV15801 + mono- Terapia)	pegasisi 180 µg+ riba- virini 800 mg 24 kvira (NV15942)	pegasisi 180 µg+ riba-virini 1000- 1200 mg 48 kvira (NV15801 + NV15942)	inter-feron alfa2b 180 µg+ riba-virini 1000-1200 mg 48 kvira (NV15801)	pegasisi 180 µg+ riba- virini 800 mg 24 kvira pegasisi 180 µg+ riba-virini 800 mg 24 kvira	pegasisi 180 µg+ riba- virini 1000-1200 mg 72 kvira (MV17150)
	<b>N=448</b>	<b>N=827</b>	<b>N=207</b>	<b>N=827</b>	<b>N=443</b>	<b>N=288</b>	<b>N=156</b>
	%	%	%	%	%	%	%
<i>metaboluri da kvebis darRvevebi</i>							
anoreqisia	13	16	20	27	26	23	15
wonis kleba	4	5	2	7	10	16	9
<i>fsiqiatriaული darRvevebi</i>							
uZiloba	6	20	30	32	37	19	29
depresia	4	18	17	21	28	22	16
gaRizianeba	3	17	28	24	27	15	17
koncentraciis unaris daqveiTeBa	2	9	8	10	13	2	5
aforiaqeba	3	6	8	8	12	8	6
<i>nervuli sistemis darRvevebi</i>							
Tavis tkivili	23	52	48	47	49	35	32
Tavbrusxveva vertigos CaTvliT	6	15	13	15	15	7	10
<i>respiratoruli sistema</i>							
qoSini	1	5	11	13	14	7	11
xvela	2	4	8	13	7	3	17
<i>saWmlis momnelebeli sistema</i>							
gulisreva	6	24	29	28	28	24	24
faRaraTi	6	16	15	14	10	16	13
muclis tkivili	4	15	9	10	9	7	9
<i>kani da kanqveSa qsovili</i>							
alopecia	17	23	25	24	33	10	18
qavili	6	13	25	21	18	5	22
dermatiti	<1	9	15	16	13	1	1
kanis simSrale	1	5	13	12	13	4	17
<i>Zval-saxsrovani sistema</i>							
mialgia	25	37	42	38	49	32	22
arTralgia	10	26	20	22	23	16	15
<i>sxvadasxva</i>							

daRliloba	21	49	45	49	53	40	36
temperaturuli reakcia	52	35	37	39	54	41	20
	6	30	30	25	34	16	12
infeqcia	7	22	28	21	16	10	12
tkivili	1	11	9	10	9	6	6
asTenia	11	7	18	15	16	26	30

- klinikur kvlebebSi 450 pacienti mkurnalobda pegasisi+lamivudiniT. danarCen SemTxvebebSi lamivudins pegasisis usafrTxoebis profilze gavlena ar hqonia.

gverdiTi efeqtebi 1%-ze meti da 10%-ze naklebi sixSiriT, romlebic gamovlinda B hepatitis, C hepatitis da aiv+ C hepatitis virusis koinfeqciis pegasisis monoTerapiis an kombinirebulii Terapiis saxiT mkurnalobisas:

*infeqciebi:* martivi herpesi, saSarde gzebis infeqciebi, bronqiti, kandidozi.

*hematologiuri da limfuri sistema:* limfadenopaTia, anemia, Trombocitopenia

*endokrinuli sistema:* hipoTireoidizmi, hiperTireoidizmi.

*nervuli sistemisa da fsiqiatრიული darRvevebi:* mexsierebis daqveiTeba, gemos SegrZnebis darRveva, paresTezia, hiperesTezia, tremori, sisuste, emociuri aSlilobebi, xasiaTis clileba, nevrozi, agresia, libidos daqveiTeba, Sakiki, somnolencia, koSmarebi, sinkope.

*ofTalmologiuri movlenebi:* mxedvelobis dabindva, qserofTalmia, Tvalis anTebiTi daavadebebi, yuri da labirinTi: vertigo, yuris tkivili

*gul-sisxlZarRvTa sistema:* gulis friali, periferiuli SeSupeba, taqikardia

*sisxlZarRvebis dazianeba:* SewiTlebebi

*respiratoruli sistema:* yelis tkivili, riniti, nazofaringiti, sinusebis SeSupeba, cxviridan sisxldena, qoSini datvirTvisas

*gastro-intestinuri sistemis darRvevebi:* Rebineba, dispefsia, meteorizmi, piris simSrale, piris Rrus dawyluleba, RrZilebidan sisxldena, stomatiti, disfagia, glositi.

*kani da kanqveSa qsovili:* kanis dazianeba, siwiTle, egzema, fsoriazi, urtikaria, fotomgrZnobelobis reakciebi, oflianoba, Ramis oflianoba

*Zval-kunTovani da SeamaerTebelqsovilovani sistema:* Zvlebis, zurgis, kisoris tkivili, kunTebis krampebi, kunTovani sisuste, Zvlebisa da kunTebis tkivili, arTriti

*reproduqciuli sistema da sarZeve jirkvlebi:* impotencia.

*sxvadasxva:* gripismagvari daavadeba, leTargia, wamoxureba, tkivili gulmkerdSi, wyurvilis gaZliereba,

gverdiTi efeqtebi 1%-ze meti da 2%-ze naklebi sixSiriT, romlebic gamovlinda aiv+ C hepatitis virusis koinfeqciis pegasisi+ribaviriniT mkurnalobisas iyo: hiperlaqtacidemia, laqtaturi acidozi, gripi, pnevmonia, afeqturi reakciebi, apaTia, tinitusi, xaxisa da xorxis tkivili, qeiliti, SeZenili lipodistrofia da qromaturia. sxva alfa interferonebis msgavsad pegasisi/ribavirini an pegasisiT mkurnalobas SeiZleba Tan axldes naklenad damaxasiaTebeli-iSviaTi gverdiTi efeqtebi: qveda sasunTqi gzebis infeqciebi, kanis infeqciebi, otiti, endokarditi, suicidi, dozis gadaWarbeba, RviZlis funqciis darRveva, RviZlis gaximovneba, qolangiti, RviZlis avTvisebiani neoplazia, kuWisa da 12goja nawlavis wylulovani daavadeba, gastro-intestinuri sisxldena, pankreatiti, sxvadasxva ariTmia, maT Soris mocimcime ariTmia, perikarditi, autoimunuri daavdebebi (mag. idiopaTiuri Trombocitopeniuri purpura, fsoriazi, revmatoiduli arTriti, wiTeli mglura), mioziti, periferiuli neiropaTia, sarkoidozi, fataluri intersticiuli pnevmoniti, filtvis arteriis Tromboembolia, rqovanas dawyluleba, cerebruli hemoragia, Trombozuli Trombocitopeniuri purpura, fsiqozuri aSliloba, halucinaciebi.

sxva alfa interferonebis msgavsad, pegasisi+kopegusiT mkurnalobisas iSviaTad SeiZleba gamovlindes pancitopenia da aplaziuri anemia.

### 2.6.1.1 laboratoriuvi cvlilebebi

C hepatitis kombinaciuri mkurnalobisas ixileT aseve ribavirinis instrucia da ribavirinis moqmedeba laboratoriu parametrebze.

#### *hematologia*

sxva alfa-interferonebis msgavsad, pegasisiTa da pegasisi/ribaviriniT mkurnalobisas aRiniSneba hematologiuri maCveneblebis raodenobrivi Semcireba, rac ZiriTadad Seqcevadia dozis Semcirebis Sedegad da mkurnalobis Sewyvetidan 4-8 kviraSi ubrundeba sawyis maCveneblebs.(ix.2.4 gafrTxileba da sifrTxilis zomebi da 2.2.1 dozirebis instruciebi gansakuTrebul SemTxvevebSi). Trombocitopenia da anemia ZiriTadad vlindeba aiv+ C hepatitis virusis koinfeqciis dros.

am cvlilebebis umetesobis ukuganviTareba xdeba dozis Semcirebis da zrdis faqtorebis miRebiT da iSviaTad saWiroebs mkurnalobis Sewyvetas.

#### *hemoglobini da hematokriti*

C hepatitis pegasisiT monoTerapiis dros pacientTa mxolod 1 %-s , maT Soris pacientebis cirozis diagnoziT, aReniSnebaT hemoglobinisa da hematokritis Semcireba da esaWiroebaT preparatis dozis modifitseba(Semcireba). pegasisi+ 1000/1200 mg ribaviriniT mkurnalobisas pacientTa daaxloebiT 10%-s mkurnalobis 48 kviraze esaWiroeba preparatis dozis Semcireba anemiis gamo. aiv+ C hepatitis virusis koinfeqciis dros pegasisiT monoTerapiis da pegasisi/ribaviriniT mkurnalobisas anemia (<10g/dl) aReniSna 7% da 14%-Si Sesabamisad.

#### *leikocitebi*

pegasisiT mkurnalobisas mcirdeba leikocitebisa da neutrofilebis raodenoba. neutrofilebis ricxvis Semcireba 500 ujrudi/mm<sup>3</sup>-mde gamovlinda pegasisiT mkurnalobisas B hepatitis mqone pacientebis 4%-Si, pegasisi/ribaviriniT mkurnalobisas ki C hepatitis 5%-Si. aiv+C hepatitis virusis koinfeqciis dros neutrofilebis ricxvis Semcireba 500 ujrudi/mm<sup>3</sup>-mde 13% da 11 % Si Sesabamisad pegasisi monoTerapiiT da kombinaciuri mkurnalobis dros.

#### *Trombocitebi*

klinikur kvlebebSi C hepatitis pegasisiT mkurnalobisas Trombocitebis ricxvis Semcireba 50000 ujrudi/mm<sup>3</sup>-mde aRiniSna 5%-Si, rac ZiriTadad gamovlinda RviZlis ciroziT garTulebis mqone da pacientTa im jgufSi, romelTa SemTxvevaSiC kvlebaSi CarTvisas Trombocitebis ricxvi Seadgenda 75000 ujrudi/ mm<sup>3</sup> an ufro naklebs. B hepatitis SemTxvevaSi Trombocitebis ricxvis Semcireba 50000 ujrudi/mm<sup>3</sup>-de aReniSna klinikur kvlebebSi CarTul pacientebis sawyisi TrombocitopeniiT. aiv+ C hepatitis virusis koinfeqciis dros Trombocitebis ricxvis Semcireba 50000 ujrudi/mm<sup>3</sup>-de aRiniSna 10% da 8%- Si pegasisiT monoTerapiis da pegasisi/ ribaviriniT mkurnalobisas Sesabamisad.

#### *farisebri jirkvlis funqciebi*

pegasisiT mkurnalobisas SeiZleba gamovlindes farisebri funqciis klinikurad mniSvnelovani darRvevebi. (ix.2.4.) pegasisiT mkurnalobis fonze gamovlenili farisebri jirkvlis funqciis darRvevebis sixSire iseTivea, rogorc sxva interferonebiT mkurnalobisas.

#### *Trigliceridebi*

interferoniT da Sesabamisad pegasisiT mkurnalobisas aRiniSneba trigliceridebis donis mateba.

#### *anti-interferonuli anitixeulebi*

pegasisiT an pegasisi/ribaviriniT mkurnalobisas interferonis sawinaaRmdego antisxeulebis dabali titri gamovlinda C hepatitisian pacientebis 3%-Si(25/835). antisxeulebis paTologiur-klinikuri mniSvneloba ar aris cnobili. Aaseve, ar aRiniSneboda korelacia interferonis sawinaaRmdego antisxeulebis warmoaqmnasa da mkurnalobis efeqturobas an gverdiTi efeqtibus ganviTarebas Soris.

### **2.6.2.postmarketinguli monacemebi**

pegasisiTa da ribaviriniT mkurnalobisas postmarketingul periodSi calkeul SemTxvevebSi gamovlinda multiformuli eriTema, stivens-jonsonis sindromi - toqsiuri epidermul nekrolizi, wiTeli ujrerebis aplazia PRCA da suicidis azrebi. dehidraciis SemTxvevebi gamovlinda iSviaTad. Aaseve, sxva interferonebiT mkurnalobis msgavsad, pegasisisa da kopegusiT mkurnalobisas aRiniSna baduris aSrebebis SemTxvevebi. sxva interferonebiT mkurnalobis

msgavsad, pegasisiT monoTerapiis an kopegusTan kombinaciuri mkurnalobisas aRiniSna RviZlisa da Tirkmlis transplantatis mocilebis reaqciebi.

## **2.7. Warbi dozireba**

aRwerilia erTkviriani intervalis nacvlad or dReSi ori ineqciis da yoveldRiurad erTi kviris ganmavlobaSi preparatis gamoyeneba saerTo doziT \_ 1260 mkg/kviraSi. raime seriozuli gverdiTi movlena ar aris registrirebuli. pegasisi Tirkmlis karcinomisa da qronikuli mieloiduri leukemiis dros kvlebebSi gamoyenebulia 540-630 mkg/kviraSi doziT Sesabamisad. Warbi doziT miRebasTan dakavSirebuli gverdiTi efeqtobia: daRliloba, RviZlis fermentebis mateba, neutropenia da Trombocitopenia. klinikur kvlebebSi ar dafiqsirebula dozis gadaWarbebis SemTxveva. ixileT ribavirinis gamoyenebis instruqcia.

## **3.farmakologiuri moqmedeba da farmakologiuri maxasiaTeblebi**

### **3.1 farmakodinamikuri Tvisebebi**

PEG reagentis (bi-monomeT-oqsipolieTilen-glikoli) interferon alfa2 a -sTan koniugaciiT miiReba pegilirebuli alfa2 a interferoni. pegilirebuli alfa2 a interferonis miReba xdeba biosinTezis gziT rekombinantuli dnm teqnologiis gamoyenebiT da warmoadgens produqts, romlis sinTezi xdeba *E. coli* -Si CaSenebuli adamianis klonirebuli leukocitebis interferonis eqspresirebuli geniT. PEG reagentis struqtura pirdapir gavlenas axdens pegasisis farmakologiaze. kerZod, PEG nawilakis zoma (40kda), da gantoteba ganapirobebs mis Sewovas, ganawilebas da eliminacias. ribavirinis farmakodinamikuri maxasiaTeblebis Sesaxeb informacia ixileT ribavirinis sainformacio bukletSi.

#### **3.1.1. moqmedebis meqanizmi**

pegasisi *in vitro* avlens interferon alfa2a-s antivirusul da antiproliferaciul Tvisebebs. interferoni urTierTqmedebis ujredis zedapirze ganlagebul specifiur receptorebTan, riTic iwyeba rTuli ujredSida signalis gadacema da genis transkripciiis swrafi gaaqtiveba.

interferonis mier gaaqtivebuli geni iwvevs mraval biologiuur efeqts da maT Soris inficirebul ujredSi virusis replikaciiis da ujredobis proliferaciiis inhibirebas da imunomodulacias. pegasisis miRebisas qr. C hepatitis dros C hepatitis virusis rnm-is cvlileba xdeba or fazad. C hepatitis virusis rnm-is pirveli Semcireba aRiniSneba pegasisis pirveli dozis miRebidan 24-36 sT-Si. meored Semcireba aRiniSneba myari virusuli pasuxis SemTxvevaSi pegasisiT mkurnalobidan 4-16 kviraSi. pegasisi 180 mkg/kviraSi doziT standartul alfa interferonTan SedarebiT aumjobesebs virusul pasuxs da mkurnalobis Sedegs. pegasisi astimulirebs efeqtori proteinebis Sratiss neopterinisa da 2',5'-oligoadenilatsinTazas da rac doza-damokidebuli procesia. 2',5'-oligoadenilatsinTazas maqsimaluri sinTezi xdeba pegasisis 135-180 mkg/kviraSi dozirebisas da misi koncentracia maqsimaluri rCebaMmTeli kviris ganmavlobaSi. 2',5'-oligoadenilatsinTazas sinTezi da aqtivoba Semcirebulia 62 welze meti asakis pacientebSi da Tirkmlis funqciis mniSvnelovani darRvevis dros kerZod, kreatininis klirensi Seadgens 20-40ml/wT. am monacemebis Sesabamisoba pegasisis farmakodinamikuur markerebTan ar aris cnobili

#### **3.1.2. klinikuri efeqturobis kvlebebi**

##### **B hepatitis**

klinikurma kvlebebma aCvena, rom pegasisi monoTerapiis saxiT efeqturia rogorc HBeAg -dadebiTi, ise HBeAg-uaryofiTi-anti HBeAg-dadebiTi formis qronikuli B hepatitis SemTxvevaSi

##### *klinikuri efeqturobis damadasturebeli klinikuri kvlebebi*

kvlebebSi CarTuli iyvnen pacientebi qronikuli B hepatitisiT, B hepatitis virusis dnm-is aqtiuri replikaciiT, alaninaminotransferazis momatebuli doniT da RviZlis biofsiiT gamovlenili qronikuli hepatitis suraTiT. WV16240kvlevaSi CarTuli iyo HBeAg -dadebiTi pacientebi, WV16241 kvlevaSi ki pacientebi HBeAg-uaryofiTi - anti HBeAg-dadebiTi testiT. orive kvlevaSi

mkurnaloba grZeldeboda 48 kviris ganmavlobaSi da mkurnalobis dasrulebis Semdeg dakvirveba grZeldeboda 24 kviris ganmavlobaSi. orive kvlevaSi xdeboda pegasisisa da placebos, pegasisisa da lamivudinis kombinaciis lamivudinis monoTerapiasTan Sedareba. kvlebebSi ar iyvnen CarTuli pacientebi aiv+ B hepatitis koinfeqciiT. virusuli pasuxi orive kvlevis jgufebSi motanilia cxrilSi 4. B hepatitis virusis dnm-is gansazRvra xdeboda Cobas Amplicor meTodiT (deteqciis zRvari 100 erTeuli/ml).

**cxrili 4. serologiuli, virusuli da bioqimiuri pasuxi B hepatitis mkurnalobis dros**

	WV16240kvleva HBeAg –dadebiTi pacientebi			WV16241 kvleva HBeAg-uaryofiTi - anti HBeAg-dadebiTi pacientebi		
	pegasisi 180 mkg da placebo (N=271)	pegasisi 180 mkg da lamivudini 100 mg (N=271)	lamivudini 100 mg (N=272)	pegasisi 180 mkg da placebo (N=177)	pegasisi 180 mkg da lamivudini 100 mg (N=179)	lamivudini 100 mg (N=181)
HBeAg serokonversia	32% <sup>1</sup>	27%	19%	ar Catarebula	ar Catarebula	ar Catarebula
B hepatitis virusis dnm *	32% <sup>2</sup>	34%	22%	43% <sup>5</sup>	44%	29%
ALT –s normalizacia	41% <sup>3</sup>	39%	28%	59% <sup>6</sup>	60%	44%
HBsAg serokonversia	3% <sup>4</sup>	3%	0%	3%	2%	0%

\* HBeAg-dadebiTi pacientebisaTvis: B hepatitis virusis dnm <105 erT/ml

HBeAg-uaryofiTi - anti HBeAg-dadebiTi pacientebisaTvis: B hepatitis virusis dnm <2 x 10<sup>4</sup> erT/ml

1 Sefardeba (95% CI) vs. lamivudini = 2.00 (1.34 – 2.97), p(kohran-mantel-henszelis testiT) <0.001

2 Sefardeba (95% CI) vs. lamivudini = 1.64 (1.12 – 2.42), p(kohran-mantel-henszelis testiT) = 0.012

3 Sefardeba (95% CI) vs. lamivudini = 1.77 (1.23 – 2.54), p(kohran-mantel-henszelis testiT) = 0.002

4 Sefardeba –gansazRvrevlia. p(kohran-mantel-henszelis testiT) = 0.004

5 Sefardeba (95% CI) vs. lamivudini = 1.84 (1.17 – 2.89), p(kohran-mantel-henszelis testiT) = 0.007

6 Sefardeba (95% CI) vs. lamivudini = 1.86 (1.22 – 2.85), p(kohran-mantel-henszelis testiT) = 0.004

**C hepaiti**

klirikuri kvlebebiT dadasturebulia, rom pegasisi monoTerapiis saxiT an kopegusTan (ribavirini) kombinirebuli mkurnalobisas efeqturia qronikuli C hepatitis maT Soris RviZlis kompensirebuli cirozis da aiv+ C hepatitis koinfeqciis dros

*efeqturobis damadasturebeli klinikuri kvlebebi aranamkurnaleb axladdiagnostirebul pacientebSi*

kvlebebSi CarTuli iyvnen pacientebi qronikuli C hepaitiT, gansazRvradi HCV rnm-iT, alaninaminotransferazis momatebuli doniT da RviZlis biofsiT gamovlenili qronikuli hepaitiT.

NV15495 kvlevaSi CarTuli iyvnen pacientebi cirozis histologiuri (80%) diagnoziT an cirozis gardamavali formiT (20%). kvlevaSi CarTuli pacientebis mkurnaloba, mkurnalobis xangrZlivoba da gamosavali ix,. cxrilebSi 5 da 6. virusul pasuxad iTvleba aragansazRvradi HCV rnm gansazRvruli Cobas Amplicor meTodiT, versia 2.0 (deteqciis zRvari 100 erTeuli/ml eqivalenti- 50 IU/ml). myar virusuli pasuxad iTvleba aragansazRvradi HCV rnm-is gamovlena mkurnalobis dasrulebidan 6 Tvis Semdeg.

**cxrili 5. virusuli pasuxi qronikuli C hepatitis dros**

	monoTerapia pegasisiT		kombinarebuli Terapia pegasusiT
	pacientebi ciroziT da cirozis gareSe	pacientebi ciroziT	pacientebi ciroziT da cirozis gareSe



	NV15496 + NV15497 + NV15801 kvleva		NV15942 kvleva		NV15942 kvleva	NV15801 kvleva	
	pegasisi 180 mg  N=701 48 kvira	interferoni alfa 2a 6MIU 3MIU da 3MIU  N=478 48 kvira	NV15942 kvleva  N=87 48 kvira	interferoni alfa 2a 3MIU  N=88 48 kvira	NV15942 kvleva  da ribavirini 1000-1200mg  N=436 48 kvira	NV15942 kvleva  da ribavirini 1000-1200mg  N=453 48 kvira	interferoni alfa 2b 3MIU da ribavirini 1000-1200mg  N=444 48 kvira
virusuli pasuxi mkurnalobis bolos	55 - 69%	22 - 28%	44%	14%	68%	69%	52%
sabooloo myari virusuli pasuxi	28 - 39%	11 - 19%	30%*	8%*	63%	54%**	45%**
95% CI: 11% - 33%, p ≤0.001(kohran-mantel-henszelis testi)							
95% CI: 3% - 16%, p ≤0.003(kohran-mantel-henszelis testi)							

pegasisiTa da ribavirinis kombinirebuli mkurnalobis Sedegad miRweuli virusuli pasuxi virusul datvirTvasa da genotipTan dakavSirebiT mocemulia cxrilSi #6. NV15942kvlevis monacemebi izleva preparatis racionaluri arCevis SesaZleblobas virusis genotipis mixedviT (ix. crili#1). genotipis mixedviT preparatis mimarT mgrZnobelobaze gavlenas ar axdenda sawyisi virusuli datvirTva an cirozis arseboba/ararseboba. Aamdenad, genotipi 1, 2 da 3 C hepatitis mkurnalobasTan dakavSirebuli rekomendaciebi ar aris damokidebuli am sawyis maxasiaTeblebze.

**cxrili. 6 myari virusuli pasuxi qronikuli C hepatitis dros genotipisa da sawyisi virusuli datvirTvis mixedviT pegasisis da ribavirinis kombinirebuli mkurnalobis SemTxvevaSi.**

	NV15942 kvleva			NV15801 kvleva		
	pegasisi 180 mkg da ribavirini 800mg 24 kviris ganmav-lobaSi	pegasisi 180 mkg da ribavirini 1000-1200mg 24 kviris ganmav-lobaSi	pegasisi 180 mkg da ribavirini 800mg 48 kviris ganmav-lobaSi	pegasisi 180 mkg da ribavirini 1000-1200mg 48 kviris ganmav-lobaSi	pegasisi 180 mkg da ribavirini 1000-1200mg 48 kviris ganmav-lobaSi	interferon alfa2b3 MIU da ribavirini 1000-1200mg 48 kviris ganmav-lobaSi
genotipi1	29% (29/101)	42% (49/118)*	41% (102/250)*	52% (142/271)*	45% (134/298)	36% (103/285)
maRali virusuli datvirTva	41% (21/51)	52% (37/71)	55% (33/60)	65% (55/85)	53% (61/115)	44% (41/94)
dabali virusuli datvirTva	16% (8/50)	26% (12/47)	36% (69/190)	47% (87/186)	40% (73/182)	33% (62/189)
genotipi2,3	84% (81/96)	81% (117/144)	79% (78/99)	80% (123/153)	71% (100/140)	61% (88/145)
maRali virusuli datvirTva	85% (29/34)	83% (39/47)	88% (29/33)	77% (37/48)	76% (28/37)	65% (34/52)

dabali virusuli datvirTva	84% (52/62)	80% (78/97)	74% (49/66)	82% (86/105)	70% (72/103)	58% (54/93)
genotipi 4	(0/5)	(8/12)	(5/8)	(9/11)	(10/13)	(5/11)

\* pegasisi 180 mkg da ribavirini 1000-1200mg 48 kviris ganmav-lobaSi vs. pegasisi 180 mkg da ribavirini 800mg 48 kviris ganmav-lobaSi 95% CI: 1.52 (1.07-2.17),  $p \leq 0.003$  (kohran-mantel-henszelis testi)

\* pegasisi 180 mkg da ribavirini 1000-1200mg 48 kviris ganmav-lobaSi vs. pegasisi 180 mkg da ribavirini 800mg 24 kviris ganmav-lobaSi 95% CI: 2.12 (1.3-3.46),  $p \leq 0.002$  (kohran-mantel-henszelis testi)

klirikuri kvlebebiT dadgenilia, rom pegasisi interferon-alfa-2a-Tan SedarebiT avlens met efeqturobas rogorc histologiuri pasuxis mxriv pacientebSi cirozis diagnoziT, aseve aiv+ C hepatitis koinfeqciis dros. mkurnalobis kursis 24 kviramde Semoklebis SesaZlebloba Seswavlili iqna NV15942 kvlebebiSi 1 da 4 genotipis pacientebSi, romelTac hqondaT swrafi myari virusuli pasuxi mkurnalobis meoTxe kviris Semdeg (ix. cxrili 7).

**cxrili 7. myari virusuli pasuxi swrafi virusuli pasuxis Semdeg mkurnalobis meoTxe kviris Semdeg pegasisisa da ribavirinis kombinirebuli mkurnalobis SemTxvevaSi.**

NV15942 kvleba		
	pegasisi 180 mkg da riba-virini 1000-1200mg 24 kviris ganmav-lobaSi	pegasisi 180 mkg da ribavirini 1000-1200mg 24 kviris ganmav-lobaSi
genotipi 1 swrafi virusuli pasuxiT	90% (28/31)	92% (47/51)
dabali virusuli datvirTva	93% (25/27)	96% (26/27)
maRali virusuli datvirTva	75% (3/4)	88% (21/24)
genotipi 1 swrafi virusuli pasuxis gareSe	24% (21/87)	43% (95/220)
dabali virusuli datvirTva	27% (12/44)	50% (31/62)
maRali virusuli datvirTva	21% (9/43)	41% (64/158)
genotipi 4 swrafi virusuli pasuxiT	(5/6)	(5/5)
genotipi 4 swrafi virusuli pasuxis gareSe	(3/6)	(4/6)

dabali virusuli datvirTva =  $\leq 800,000$  IU/ml;

maRali virusuli datvirTva =  $> 800,000$  IU/ml;

swrafi virusuli pasuxi (aragansazRvradi HCV rnm-) mkurnalobis dawyebidan 4 da 24 kviris Semdeg.

mkurnalobis kursis 16 kviramde Semoklebis SesaZlebloba Seswavlili iqna NV17317 kvlebaSi 2 da 3 genotipis pacientebSi, romelTac hqondaT swrafi myari virusuli pasuxi mkurnalobis meoTxe kviris Semdeg (ix. cxrili #8). NV17317 kvlebaSi pacientebi 2 da 3 genotipis 2 da 3 genotipis virusiT itarebdnen kombinirebul Terapias pegasisi 180 mkg/kviraSi+ribavirini 800 mg dReSi da dayofilni iyvnen 2 jgufad- 16 da 24 kviriani mkurnalobis jgufebad. 16 da 24 kviriani mkurnalobisas erTaniri virusuli pasuxi ar iyo miRweuli. (ix. cxrili #8). 16 kviris ganmavlobaSi Catarebuli mkurnalobisas aRiniSna dabali sixSire (65%) 24 kvirian mkurnalobasTan SedarebiT (76%).

im pacientebis retrospektuli analiziT, romelTac hqondaT dabali sawyisi virusuli datvirTva da aragansazRvradi HCV rnm, mkurnalobidan meoTxe kviris Semdeg dadginda, rom myari virusuli pasuxi 16 da 24 kviriani mkurnalobis jgufebSi Seadgenda Sesabamisad 89% da 94%-s (ix. cxrili 8).

**cxrili 8. swraf virusul pasuxze dafuZnebuli myari virusuli pasuxi  
mkurnalobidan meoTxe kviris Semdeg 2 da 3 genotipis C  
hepatitis virusis dros pegasisisa da ribavirinis kombinirebuli mkurnalobisas  
NV17317kvlevaSi.**

NV17317 kvleva		
	pegasisi 180 mkg da ribavirini 800mg 16 kviris ganmav-lobaSi	pegasisi 180 mkg da ribavirini 800mg 24 kviris ganmav-lobaSi
genotipi 2 an 3	65% (443/679)	76% (478/630)
genotipi 2 an 3 swrafi virusuli pasuxiT	82% (378/461)	90% (370/410)
dabali virusuli datvirTva	89% (147/166)	94% (141/150)
maRali virusuli datvirTva	78% (231/295)	88% (229/260)
genotipi 2 an 3 swrafi virusuli pasuxis gareSe	30% (65/218)	49% (108/220)
dabali virusuli datvirTva	44% (22/50)	50% (25/50)
maRali virusuli datvirTva	26% (43/168)	49% (83/170)

dabali virusuli datvirTva =  $\leq$  800,000 IU/ml;

maRali virusuli datvirTva =  $>$  800,000 IU/ml;

swrafi virusuli pasuxi (aragansazRvradi HCV rnm) mkurnalobis dawyebidan 4 Semdeg.

**pegilirebuli interferon alfa2b + ribaviriniT Catarebuli mkurnalobis mimarT rezistentuli qronikuli C hepatitis**

MV17150 kvlevaSi CarTuli iyvnen pacientebi qr. C hepatitiT, romelTac ar aReniSnaT virusuli pasuxi pegilirebuli interferon alfa2b+ ribaviriniT mkurnalobisas. pacientebi daiyo 4 jgufad: I jgufi- pegasisi 360 mkg/kviraSi 12 kviris ganmavlobaSi, ESemdeg 180 mkg/kviraSi 60 kviris ganmavlobaSi. II jgufi- pegasisi 360 mkg/kviraSi 12 kviris ganmavlobaSi, ESemdeg 180 mkg/kviraSi 36 kviris ganmavlobaSi. III jgufi- pegasisi 180 mkg/kviraSi 72 kviris ganmavlobaSi. IV jgufi- pegasisi 180 mkg/kviraSi 48 kviris ganmavlobaSi. oTxive jgufs paralelurad utardeboda mkurnaloba ribaviriniT 1000-1200 mg/dReSi. pacientebze dakvirveba xdeboda mkurnalobis dasrulebidan 24 kviris ganmavlobaSi. stabiluri virusuli pasuxis damokidebuleba pegasis dozirebasTan mocemulia cxrilSi 9.

**cxrili 9. stabiluri virusuli pasuxi pegilirebuli interferon  
alfa2b+ribaviriniT Catarebuli mkurnalobis mimarT rezistentuli qronikuli C  
hepatitis dros**

MV17150				
	72 kviriani jgufebi N=473	48 kviriani jgufebi N = 469	360 mkg-jgufebi N = 473	180 mkg-jgufebi N = 469
stabiluri virusuli pasuxi	16%*	8%*	13%	10%

\*sarwmunoebis intervali (95%)-1.40-3.52, p = 0.00061

stabiluri virusuli pasuxi pegasisisiT mkurnalobis jgufebSi ufro xSiri iyo 48 kvirian jgufebTan SedarebiT. MV17150 kvlevaSi stabiluri virusuli pasuxis gansxvavebuli maCveneblebi mkurnalobis xangrZlivobisa da demografiuli maxasiaTeblebis mixedviT mocemulia cxrilSi 10.

**cxrili 10. pegasisiTa da ribaviriniT mkurnalobis Sedegad miRebuli stabiluri virusuli pasuxi pegilirebuli interferoni alfa2b+ribavirinis kombinaciis mimarT rezistentul pacientebSi**

	alfa2b+ribavirinis kombinirebuli kursis mimarT rezistentuli pacientebi, romelTac utardebodaT xelaxali mkurnaloba 48 kviris ganmavlobaSi % (N)	alfa2b+ribavirinis kombinirebuli kursis mimarT rezistentuli pacientebi, romelTac utardebodaT xelaxali mkurnaloba 72 kviris ganmavlobaSi % (N)
alfa2b+ribavirinis kombinirebuli mkurnalobis mimarT rezistentuli pacientebis saerTo raodenoba	8% (38/469)	16% (74/473)
genotipi 1/4	7% (33/450)	15% (68/457)
genotipi 2/3	25% (4/16)	33% (5/15)
genotipi		
1	7% (31/426)	14% (60/430)
2	0 (0/4)	33% (1/3)
3	33% (4/12)	33% (4/12)
4	8% (2/24)	30% (8/27)
sawyisi virusuli datvirTva		
maRali virusuli datvirTva (>800,000 IU/ml)	7% (25/363)	12% (46/372)
dabali virusuli datvirTva(<=800,000 IU/ml)	13% (11/84)	31% (27/86)

HALT-C kvlevaSi CarTuli iyvnen pacientebi qronikuli C hepatitiTa da RviZlis fibroziT, romelTac aReniSnaT rezistentoba alfa interferonis an pegilirebuli alfa interferonis monoTerapiis an ribavirinTan kombinirebuli Terapiis mimarT. pacientebS CautardaT 180 mkg pegasisis/kviraSi+ 1000-1200 mg ribavirini dReSi kursiT mkurnaloba. 20 kviriani mkurnalobis Semdeg im pacientebS, romelTac sixlSi aRar aRmoaCndaT C hepatitis virusi, gaugrZeldaT igive mkurnaloba 48 kviramde. mkurnalobis dasrulebis Semdeg 24 kviris ganmavlobaSi grZeldeboda dakvirveba. myari virusuli pasuxi damokidebuli iyo mkurnalobaze, romlis mimarTac pacientebi iyvnen rezistentuli. yvelaze cudi gamosavali aReniSnaT im pacientebS, romlebic rezistentulni iyvnen pegilirebuli interferonisa da ribavirinis kombinirebuli kursis mimarT. am jgufSi aRiniSna myari virusuli pasuxis iseTi sixSire, rogoric MV17150kvlevis 48 kvirian jgufSi. interferonis an pegilirebuli interferoniT monoTerapiis mimarT rezistentobis dros myari virusuli pasuxis miRweva ufro xSiria pegilirebuli interferonisa da ribavirinis kombinirebuli Terapiis mimarT rezistentul pacientebTan SedarebiT, magram mniSvelovnad naklebia aranamkurnaleb pacientebTan SedarebiT. ix. cxrili 11.

**cxrili 11. myari virusuli pasuxis ganviTarebis sixSire mkurnalobis xangrZlivobis mixedviT**

mkurnalobis xangrZlivoba	interferoni	pegilirebuli interferoni	interferoni +ribavirino	pegilirebuli interferoni +ribavirini
48 kvira	27% (70/255)*	34% (13/38)*	13% (90/692)*	11% (7/61)* 8% (38/469)**
72 kvira	-	-	-	- 16% (74)

					/473)**
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\* HALT-C kvlevis monacemebi  
 \*\* MV17150 kvlevis monacemebi

### **namkurnalebi recidiuli qronikuli C hepatitis**

kvlevaSi CarTuli iyvnen ZiriTadad I genotipis pacientebi C hepatitiT, romleTac pegilirebuli interferon alfa2a + ribavirini 48 kviriani mkurnalobis Semdeg aReniSnaT recidivi. pacientebS 72 kviris ganmavlobaSi utardebodaT mkurnaloba pegasisiT 180mkg+ wonaze gadaangariSebuli ribaviriniT dReSi an interferoniT 9 mkg/dReSi + gadaangariSebuli ribaviriniT. stabiluri visusuli pasuxi miRweuli iqna im pacientebis 42%-Si, romleTac utardebodaT mkurnaloba pegasisiT 180mkg+ wonaze gadaangariSebuli ribaviriniT dReSi.

Ria kvlevaSi, romleSic CarTuli iyo II da III genotipis pacientebi qr. C hepatitiT, romleTac pegilirebuli interferon alfa2a + ribavirini 24 kviriani mkurnalobis Semdeg aReniSnaT recidivi. pacientebS 48 kviris ganmavlobaSi utardebodaT mkurnaloba pegasisiT 180mkg/kviraSi + ribavirini 100-1200 mg (wonaze gadaangariSebiT) dReSi da dakvirvebis qveS imyofebodnen preparatis moxsnidan 24 kviris ganmavlobaSi. stabiluri visusuli pasuxi miRweuli iqna im pacientebis 64%-Si.

### **aiv+C hepatitis virusis koinfeqcia**

NR15961 kvlevaSi 860 pacienti aiv+ HCV koinfeqciiT daiyo 3 kgufad. I jgufs utardeboda mkurnaloba pegasisi 180mkg/kviraSi+placebo, II jgufs - pegasisi 180mkg/kviraSi+ kopegusi 800 mg dReSi, III jgufs - interferoni alfa-2a 3 MIU kviraSi samjer +kopegusi 800 mg/dReSi 48 kviris ganmavlobaSi da Semdeg grZeldeboda dakvirveba mkurnalobis gareSe 24 kviris ganmavlobaSi. stabiluri virusuli pasuxi samive jgufisTvis yvela tipis pacientisa da I da II genotipis SemTxvevaSi mocemulia cxrilSi 12.

### **cxrili 12. stabiluri virusuli pasuxi aiv+ HCV koinfeqciis dros**

	pegasisi 180mkg+placebo 48 kviris ganmavlobaSi	pegasisi 180mkg+ kopegusi 800 mg 48 kviris ganmavlobaSi	interferoni alfa-2a 3 MIU +kopegusi 800 mg 48 kviris ganmavlobaSi
yvela tipis pacienti	20% (58/286)*	40% (116/289)*	12% (33/285)*
I genotipi	14% (24/175)	29% (51/176)	7% (12/171)
II genotipi	36% (32/90)	62% (59/95)	20% (18/89)

\* pegasisi 180mkg + kopegusi 800 mg vs. interferoni alfa-2a 3 MIU +kopegusi 800 mg: 95% CI sxvaobisaTvis: 22% - 35%,  $p \leq 0.0001$  (kohran-mantel-henszelis testi)

\* pegasisi 180mkg + kopegusi 800 mg vs. pegasisi 180mkg: 95% CI sxvaobisaTvis 13% - 27%,  $p \leq 0.0001$  (kohran-mantel-henszelis testi)

### **3.2 farmakokinetikuri maxasiaTeblebi**

pegasisis farmakokinetika Seswavlilia janmrTel moxaliseebSi da C hepatitis virusis mtarebel pacientebSi. ix. cxrili 13. B hepatitis SemTxvevaSi aRiniSna C hepatitis analogiuri maCveneblebi

### 3.2.1. absorbcia

janmrTel moxaliseebSi 180 mikrogrami pegasisis erTjeradi kanqveSa ineqciis Semdeg sisxlis SratSi preparatis koncentraciis gansazRvra warmoebs 3-6 saaTSi. SratSi preparatis koncentraciis pikis 80% aRiniSneba 24-48 saaTSi, xolo sruli absorbcia 72-96 saaTSi. misi bioSeRwevadoba Seadgens 84%-s da, am mxriv, igi utoldeba interferon alfa-2a-s igive maCvenebls.

### 3.2.2 ganawileba

pegasisi ZiriTadad nawildeba sisxliSi da eqstracelulur siTxeSi. intravenuri Seyvanis Semdeg preparatis ganawilebis moculoba Seadgens 6 – 14 litrs. virTagvebze Catarebuli kvlevebis monacemebiT, pegasisi agreTve nawildeba RviZiSi, Tirkmelebsa da Zvlis tvinSi.

### 3.2.3.metabolizmi

pegasisis metabolizmi, rac pegasisis klirensis mTavar meqanizms warmoadgens, ar aris srulad Seswavlili.

adamianebSi pegasisis sistemuri klirensi Seadgens 100 ml/sT-Si, rac 100-er naklebia interferon alfa-2a-s klirensze. virTagvebSi Catarebulma kvlevebma aCvena, rom Tirkmelebi warmoadgenen niSandebuli pegasisis gamoyofis ZiriTad organos. pegasisi gamoiyofa, aseve, naRvlis mJavebTan erTad. SardiT gamoyofili preparatis mxolod 10 % gamoiyofa ucveleli saxiT, Tumca PEG –is naxevari metabolizmis Semdeg rCeba dakavSirebuli interferonTan.

### 3.2.4.eliminacia

janmrTel individebSi intravenurad Seyvanis Semdeg pegasisis naxeerad daSlis periodi daaxleobiT 60 sT-s Seadgens, standartuli interferonis naxeerad daSlis periodi ki 3-4 sT-ia. terminaluri naxeerad daSlis periodi kanqveS Seyvanisas ufro xangrZlivia da saSualod udris 160 sT-s (84-353sT-s). A terminaluri naxeerad daSlis periodi SeiZleba asaxavdes ara marto eliminaciis, aramed absorbcii fazasac.

pegasisis kviraSi erTxel gamoyenebisas janmrTel individebsa da pacientebSi qronikuli C hepatitiT aRiniSna AUC da Cma-is maCveneblebis zrda proporciulad. cxrilSi # 13 mocemulia pegasisis farmakokinetikuri parametrebi 180 mkg preparatis erTjeradad Seyvanisas janmrTel individebSi da 180 mkg preparatis 48 kviris ganmavlobaSi miRebisas kviraSi erTxel.

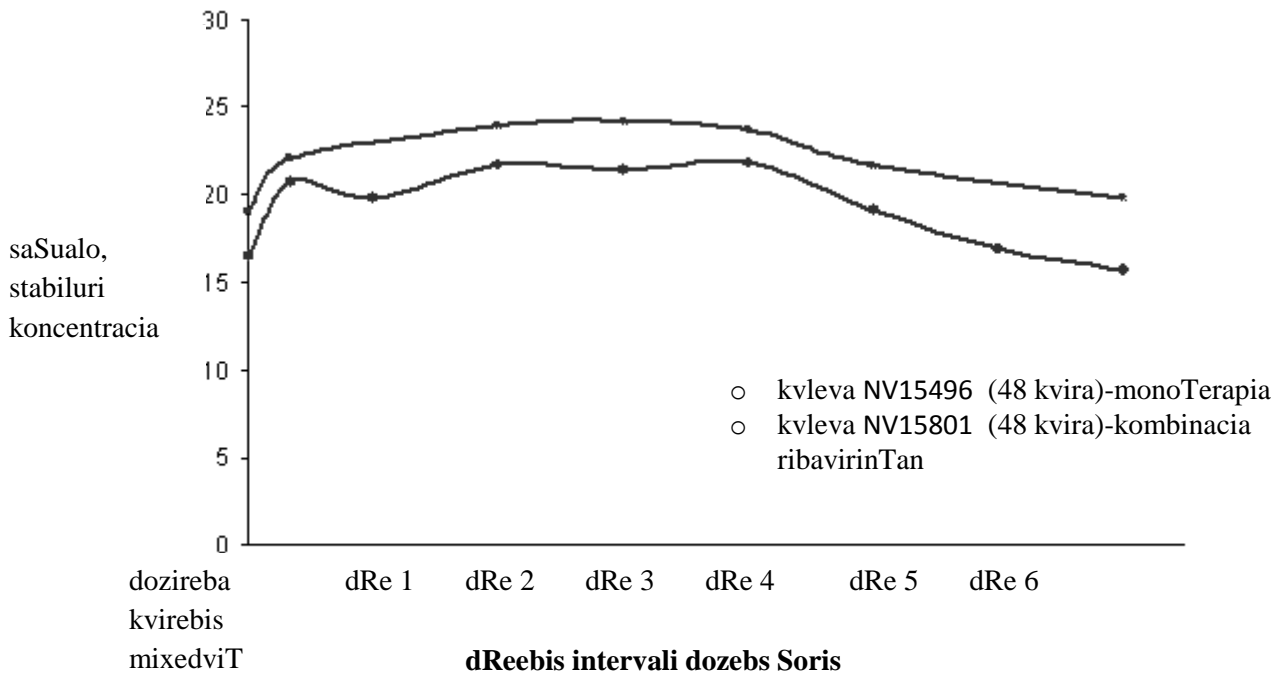
**cxrili 13. farmakokinetikuri maCveneblebi pegasisis 180 mkg erjeradi da mravaljeradi dozirebisas**

	<b>janmrTeli subieqtobi 180 mkg kanqveS (n=50)</b>	<b>qronikuli hepatitiT daavadebuli pacientebi NV15496 180 mkg kanqveS mkurnaloba (n=16)</b>	
<b>pegasisis farmakokinetikuri maCveneblebi</b>	<b>erTjeradi doza saSualo ± erTjeradi doza [zRvari]</b>	<b>erTjeradi doza saSualo ± erTjeradi doza [zRvari]</b>	<b>48kvira doza saSualo ± erTjeradi doza [zRvari]</b>
$C_{max}$ (ng/ml)	14 ± 5 [6-26]	15 ± 4 [7-23]	26 ± 9 [10-40]
$T_{max}$	92 ± 27	80 ± 28	45 ± 36

	janmrTeli subieqtebi 180 mkg kanqveS (n=50)	qronikuli hepatitiT daavadebuli pacientebi NV15496 180 mkg kanqveS mkurnaloba (n=16)	
pegasisis farmakokinetikuri maCveneblebi	erTjeradi doza saSualo ± erTjeradi doza [zRvari]	erTjeradi doza saSualo ± erTjeradi doza [zRvari]	48kvira doza saSualo ± erTjeradi doza [zRvari]
(h)	[48-168]	[23-119]	[0-97]
AUC <sub>1-168 h</sub> (ng·h/mL)	1725 ± 586 [524-3013]	1820 ± 586 [846-2609]	3334 ± 994 [1265-4824]
klirensi/F (mL/h)	94 ± 56 [34-337]	83 ± 50 [33-186]	60 ± 25 [37-142]
koncentracia 48 kviraze (ng/ml)	ar aris gamoyenebuli	ar aris gamoyenebuli	16 ± 6 [4-28]
Peak to Trough Ratio for Week 48	ar aris gamoyenebuli	ar aris gamoyenebuli	1.7 ± 0.4 [1.1-2.5]
akumulacia (AUC 48kvira/ AUC <sub>erTjeradi doza</sub> )	ar aris gamoyenebuli	ar aris gamoyenebuli	2.3 ± 1.0 [1.1-4.0]

qronikuli C hepatitiT daavadebul pacientebSi Tanabari SemanarCunebeli plazmuri koncentraciebi 2-3 jer maRalia erTjeradad gamoyenebisas miRebul koncentraciasTan SedarebiT, Tanabari SemanarCunebeli plazmuri koncentracia ki kviraSi erTxel miRebisas miiRweva preparatis miRebidan 5-8 kviraSi. Tanabari SemanarCunebeli plazmuri koncentraciis miRwevis Semdeg aRar xdeba preparatis akumulireba. pikuri maCveneblebi 48 kviriani mkurnalobis Semdeg 1.5-2/0 tolia. 2 a -peginterferonis koncentraciebi narCundebs sruli 1 kviris ganmavlobaSi (168 sT). ix. suraTi 1.

**suraTi 1: peg-interferon alfa 2-a-s koncentracia qronikuli C hepatitiT daavadebul pacientebSi 180 mkg pegasisiT monoTerapiisa (NV15496) da kopegusiT (NV15801) kombinirebuli TerapiiT**



### 3.2.5 farmakokinetika gansakuTrebul populaciaSi

#### *Tirkmlis ukmarisoba*

pegasisis farmakokinetikis mniSvnelovani gansxvaveba ar gamovlenila 23 kacian kvlevaSi Tirkmlis normaluri funqciis da Tirkmlis funqciis mniSvnelovani darRvevis mqone (kreatininis klirensi 20-100 ml/wT) or jgufs Soris. Tirkmlis daavadebis terminaluri stadiis dros pacientebSi, romelTac utardebAT hemodializi, aRiniSna preparatis klirensi 25-45 %-iT Semcireba da 135 mkg preparatis iseTive eqspozicia, rogoric aRiniSneba 180 mkg dozis miRebisas Tirkmlis normaluri funqciis dros. preparatis sawyisi dozisa da Tirkmlis funqciis darRvevis xarisxis miuxedavad Tirkmlis funqciis darRvevis dros aucilebelia patientis mkacri monitoringi da saWiroebis SemTxvevaSi pegasisis dozis Semcireba (ix.2.2. dozireba d amiRebis wesi). ix.Aaseve ribavirinis gamoyenebis instruqcia

#### *sqesi*

pegasisis farmakodinamika sxvadasxva sqesis pacientebSi ar gansxvavdeba

#### *xandazmulu pacientebi*

AUC (area under curve) ZiriTadad gazrdialia 62 welze meti asakis pacientebSi, Tumca xandazmul da 62 wlamde pacientebSi pikuri koncentraciebi Tanabaria. preparatis eqspoziciis, farmakodinamikuri pasuxisa da tolerantobis gaTvaliswinebiT xandazmul pacientebSi pegasisis Semcirebuli doziT sawyisi Terapia saWiro ar aris. (ix.2.2. dozireba da miRebis wesi).

#### *pacientebi RviZlis ciroziT da cirozis gareSe.*

pegasisis eqspozicia janmrTel individebsa da pacientebSi qronikuli B an C hepatitis diagnoziT erTmaneTisagan ar gansxvavdeboda. preparatis eqspoziciis xarisxi da farmakokinetikuri profili ar gansxvavdeboda ciroziani pacientebis, janmrTel individebisa da RviZlis kompensirebuli daavadebis mqone pacientebis jgufes Soris.



*wamlis ineqciis midamo*

pegasisis kanqveSa ineqciebis Catareba umjobesia muclis an barZayis midamoSi. kvlevebiT dadgenilia, rom pegasisis eqspozicia Semcirebulia ineqciis mxarze Catarebisas muclis an barZayis midamosTan SedarebiT.

### **3.3. pegasisis preklinikuri usafrTxoeba**

pegasisze Catarebuli preklinikuri kvlevebi interferonebis specifiurobis gamo SezRudulia. mwvave da qronikuli toqsiuroba maimunebSi alfa-2a peginterferonis mwvave da qronikuli toqsiurobis gamovlinebebi alfa – 2a interferonisagan ar gansxvavdeba.

*pegasisi+ribavirini*

ribavirinTan kombinaciaSi miRebisas maimunebSi pegasisma ar gamoiwvia ribavirinisagan gansxvavebuli sxva gverdiTi efeqti. mkurnalobasTan dakavSirebul mkveTrad gamoxatul cvlilebebs warmoadgenda gardamavali msubuqi/zomieri anemia, romlis simZimec metad iyo gamoxatuli pegasis/ribavirinis jgufSi ribavirinis monoTerapiasTan SedarebiT.

#### **3.3.1. kancerogenoba**

pegasisis kancerogenoba Seswavlili ar aris.

#### **3.3.2. mutagenoba**

Ames mutagenuri baqteriuli da *in vitro* adamianis limfocitebis qromosomuli aberaciuli gamokvlevebiT metaboluri aqtivaciis TanxlebiT da mis gareSe, pegasisis gamoyenebis SemTxvevaSi ar gamovlinda mutagenuri an klastogenuri moqmedeba ix. Aaseve, kopegusis (ribavirinis) gamoyenebis instruqcia

#### **3.3.3. moqmedeba nayofierebaze**

gverdiTi efeqtebi reproduqciuli darRvevebis saxiT Seswavlili ar aris. mdedr maimunebSi sxva alfa interferonebis msgavsad pegasisi iwvevs menstrualuri ciklis gaxangrZlivebas.

#### **3.3.4. teratogenoba**

alfa-2 a interferoniT mkurnalobisas maimunebSi orsulobis Sewyvetis mxriv mniSvnelovani cvlilebebi ar gamovlenila; Mmiuxedavad imisa, rom alfa-2 a interferoniT mkurnalobisas orsuli maimunebis STamomavlebSi teratogenuli efeqtebi ar aRiniSneboda, adamianeSi analogiuri efeqtebis gamovlena ar aris gamoricxuli.

## **4.farmaceutuli maxasiaTeblesi**

### **4.1.Senaxvis vada da pirobebi**

preparati inaxeba macivarSi +2 +8°C temperaturaze. dauSvebelia misi gayinva da SenjRreva. Ppreparati inaxeba sinaTlisagan da bavSvebisagan dacul adgilas. ar SeiZleba preparatis gamoyeneba Senaxvis vadis gasvlis Semdeg. Senaxvis vada aRniSnulia kolofze.

### **4.2. gamoyenebisa da ganadgurebis specialuri instruqciebi**

parentaluri preparetebi gamoyenebamde kargad unda daTvalierdes.

*Spricebisa da nemsebis ganadgureba:*

Spricebisa da nemsebis gamoyenebis Semdeg ganadgurebis aucilebelia Semdegi instruqciebis dacva:

- dauSvebelia nemsebisa da Spricebis meored gamoyeneba;
- gamoyenebis Semdeg Spricebi da nemsebi unda moTavsdes Spricebisa da nemsebis Sesanax specialur konteinerSi basri nivTebisaTvis;

- dauSvebelia konteineris Senaxva bavSvebisaTvis xelmisawvdom adgilze;
  - dauSvebelia Spricebisa da nemsebis Sesanaxi specialuri konteineris gadagdeba sayofacxovrebo narCenebTan erTad;
  - konteinerebi unda ganadgurdes adgilobrivi moTxovnebis Sesabamisad.
- preparatis saxlSi gamoyenebis avadmyofs unda hqondes gamoyofili Spricebisa da nemsebis Sesanaxi specilauri konteineri.

*gamouyenebeli an vadagasuli preparetebis ganadgureba*

dauSvebelia preparatis moxvedra wyalSi an sayofacxovrebo nagavTan erTad. rekomendebulia, gamouyenebeli an vadagasuli preparetebis Segroveba calkeul sistemebSi.

#### **4.3.SefuTva**

- pegasisis 180mkg saineqcio Sprici 1 an 4 cali
- pegasisis 135mkg saineqcio Sprici 1 an 4 cali
- TiToeuli ampula erTjeradi doziT Seicavs 180mkg 1 an 4 cali
- TiToeuli ampula erTjeradi doziT Seicavs 135mkg 1 an 4 cali

#### **ar SeinaxoT bavSvebisaTvis xelmisawvdom adgilze.A**

versia: noemberi 2011

damzadebulia SveicariaSi

F.Hoffmann-La Roche Ltd-s mier, bazeli;

sawarmoo saiti kaizeraugsti