

duodarti
DUODART
dutasteridi-tamsulozinis hidroqloridi

xarisxobrivi da raodenobrivi Semadgenloba

yoveli peroralurad misaRebi kafsula Seicavs 0.5 mg dutasterids da 0.4 mg tamsulozinis hidroqlorids (ix. damxmare nivTierebebis CamonaTvali).

farmaceutuli forma

kafsulebi: mogrZo myar-garsiani kafsulebi yavisferi korpusiT da narinjisferi TavsaxuriT, Savi melniT dabeWdili “GS 7CZ” an “GS TEV”.

klinikuri maxasiaTeblebi

Cvenebebi

duodarti gamoiyeneba prostatitis keTilTvisebiani hiperplaziis (BPH) samkurnalod da misi progresirebis prevenciisTvis, axdens ra simptomebis Semsuბუqebas, amcirebs prostatitis zomas (mocolobas), aumjobesebs Sardis nakads da amcirebs Sardis mwvave Sekavebis (AUR) risks, da amcirebs prostatitis keTilTvisebian hiperplaziasTan (BPH) dakavSirebuli qirurgiuli Carevis saWiroebas.

dozireba da miRebis wesi

mozrdili mamakacebi (xandazmulebis CaTvliT)

duodartis rekomendebuli dozaa erTi kafsula (0.5 mg/0.4 mg) peroralurad sakvebis miRebidan daaxloebiT 30 wuTis Semdeg dRis erTsa da imave dros. kafsulebi unda gadaiylapos mTlianad, dauReWavad da gauxsnelad. dutasteridis myar-garsiani kafsulis SigTavsTan kontakტma SeiZleba gamoiwvios orofaringialური lorwovanis gaRizianeba.

Tirkmlis funqciis darRveva

Tirkmlis funqciis darRvevis gavlena dutasteridi-tamsulozinis farmakokinetikaze Seswavlili ar aris. Tumca Tirkmlis funqciis darRvevis mqone pacientebSi dozის koreqcia mosalodneli ar aris (ix. *farmakokinetika*).

RviZlis funqciis darRveva

RviZlis funqciis darRvevis gavlena dutasteridi-tamsulozinis farmakokinetikaze Seswavlili ar aris (ix. *gafrTxilebebi da usafrTxoebis zomebi da farmakokinetika*).

ukuCvenebebi

duodarti ukunaCvenebia pacientebSi, cnobili hipermgrZnobelobiT dutasteridis, 5-alfa-reduqტazas inhibitorebis, tamsulozinis hidroqloridis an preparatis nebismieri komponentis mimarT (ix. *damxmare nivTierebebis CamonaTvali*).

duodarti ukunaCvenebia qalebsa da bavSvebSi gamoyenebisTvis (ix. *orsuloba da laqტacia*).

gafrTxilebebi da usafrTxoebis zomebi

prostatitis kibo

4-wlian kvlevaSi, romelSic monawileobda 50-75 wlis asakis 8000 mamakaci, romelTa winaswari biofsiis Sedegic prostatitis kiboze iyo uaryofiTi, PSA (prostatitis specifikuri antigeni) sawyisi done - 2.5-10ng/ml (REDUCE kvleva), 1517 mamakacs daesva prostatitis kibos diagnozi. im jgufis pacientebSi, romlebic

iRebndnen *avodarts*, glisonis 8-10 xarisxis prostatitis kibos sixSire iyo ufro maRali (n=29, 0.9%) vidre placebos jgufSi (n=19, 0.6%). ar aRiniSna glisonis 5-6 an 7-10 xarisxis prostatitis kibos sixSiris zrda. mizezobrivi kavSiri *avodartsa* da maRali xarisxis prostatitis kibos Soris dadgenili ar aris. raodenobrivi disbalansis klinikuri mniSvneloba ucnobia. mamakacebSi, romlebic iReben *duodarts*, regularulad unda moxdes prostatitis kibos riskis Sefaseba PSA testis CaTvlIT.

Semdgom damatebiT 2-wlian kvlevaSi, romelSic monawileobndnen pacientebi *avodartis* qemoprevenciis (REDUCE) kvlevidan, dadasturda prostatitis kibos axali SemTxvevebis dabali sixSire (dutasteridi [n=14, 1.2%] da placebo [n=7, 0.7%]), ar gamovlenila glisonis 8-10 xarisxis prostatitis kibos axali SemTxveva.

sxva Semdgomma xangrZlivma (18 wlamde) 5-ARI (finasteridi) qemoprevenciis kvlevam aCvena, rom virTagvebSi saerTo sicocxlisunarianoba (HR 1.02, 95% CI 0.97-1.08) an sicocxlisunarianoba prostatitis kibos diagnozis Semdeg (HR 1.01, 95% CI 0.85-1.20) statistikurad mniSvnelovnad ar gansxvavdeba finasteridsa da placebos Soris.

prostatitis-specifikuri antigeni (PSA)

PSA koncentracia mniSvnelovani komponentia skringingisTvis prostatitis kibos aRmosaCenad. *duodarti* iwvevs Sratsi saSualo PSA donis daqveiTebas daaxloebiT 50%-iT 6 Tviani mkurnalobis Semdeg.

pacientebSi, romlebic iReben *duodarts* unda dadgindes PSA axali sawyisi done 6 Tviani mkurnalobis Semdeg. rekomendebulia PSA donis regularuli monitoringi SemdgomSi. dabali PSA donis nebismieri momateba *duodartiT* mkurnalobis dros SeiZleba miuTiTebdes prostatitis kibos arsebobaze an *duodartTan* araSeTavsebad Terapiaze da frTxilad unda Sefasdes im SemTxvevaSic Tu es maCveneblebi mainc normis farglebSia mamakacebisTvis, romlebic ar iReben 5-alfa reduqtazas inhibitorebs (ix. klinikuri kvlevebi). PSA monacemis interpretaciisas im pacientebSi, romlebic iReben *duodarts*, Sesadareblad unda aiRon PSA-s wina monacemebi.

duodartiT mkurnaloba ar ewinaaRmdegeba PSA gamoyenebas rogorc instrumentis, prostatitis kibos diagnostirebisTvis axali sawyisi donis gansazRvris Semdeg.

Sratsi saerTo PSA done normas ubrundeba mkurnalobis moxsnidan 6 Tvis ganmavlobaSi.

Tavisufali da saerTo PSA donis fardoba rCeba mudmivi *duodartis* gavlenis qveSac ki. Tu eqimi irCevs procentulad Tavisufal PSA prostatitis kibos diagnostikis dasaxmareblad mamakacebSi, romlebic itareben *duodartiT* mkurnalobas, misi monacemi koreqcia aucilebeli ar aris.

TiTIT reqtaluri gasinjva, iseve rogorc prostatitis kibos sxva saxis Sefaseba, unda ganxorcieldes prostatitis keTilTvisebiani simsivniT (BPH) daavadebul pacientebSi *duodartiT* mkurnalobis dawyebamde da Semdgom periodulad.

kardio-vaskularuli gverdiTi movlenebi

or 4 wlian kvlevaSi gulis ukmarisobis sixSire (gulis daavadebebis kombinirebuli termini ZiriTadad moicavs – gulis pirvelad ukmarisobas da gulis SegubebiT ukmarisobas) ufro maRali iyo subieqtebSi, romlebic iRebndnen *avodarts* da alfa-blokeris kombinacia, ZiriTadad tamsulozins, vidre pacientebSi, romlebic ar iRebndnen am kombinacias. am or kvlevaSi gulis ukmarisobis sixSire iyo dabali ($\leq 1\%$) da cvladi kvlevebs Soris. disbalansi ar aRiniSna gul-sisxlZarRvTa gverdiTi movlenebs Soris arcerT kvlevaSi. *avodarts* (marto an alfa-blokerTan kombinaciaSi) da gulis ukmarisobas Soris mizezobrivi kavSiri dadgenili ar aris (ix. klinikuri kvlevebi).

12 randomizebuli, placebo- an komparator-kontrolirebadi klinikuri kvlevebis (n=18.802) meta-analizSi, romelic afasebda kardio-vaskularuli gverdiTi movlenebis ganviTarebis risks *avodartis* gamoyenebis dros (sakontrolosTan SedarebiT), gulis ukmarisobis (RR 1.05; 95% CI 0.71, 1.57), miokardiumis mwvave infarqtis (RR 1.00; 95% CI 0.77, 1.30) an insultis (RR 1.20; 95% CI 0.88, 1.64) Tanamimdevruli statistikurad mniSvnelovani riskis mateba ar gamovlenila.

ZuZus kibo

ZuZus kibo iSviaTi SemTxvevebi aRwerilia mamakacebSi, romlebic iRebden *avodarts* klinikur kvlebebSi da post-marketingul periodSi. Tumca epidemiologurma kvlewebma gamoavlina, rom mamakacis ZuZus kibos ganviTarebis riski ar izrdeba 5-ARI-ebis gamoyenebisas. eqimebma pacientebS unda auxsnan, rom ZuZus qsovilis nebismieri cvlilebis SemTxvevaSi, rogoricaa kvanZebi an dvrilebidan gamonadeni, dauyovnebliv acnobon eqims..

hipotenzia

rogorc sxva alfa-1 adrenerguli blokerebis SemTxvevaSi, orTostatuli hipotenzia SeiZleba ganviTardes pacientebSi, romlebic mkurnaloben tamsuloziniT, ramac iSviaT SemTxvevaSi SeiZleba gamoiwvios sinkope. pacientebS, romlebic iwyeben *duodartiT* mkurnalobas unda ecnoboT, rom gamoiCinon sifrTxile dajdomis an dawolis dros orTostatuli hipotenziis pirveli niSnebisas (Tavbrusxevea da vertigo) simptomebis moxsnamde.

sifrTxilea saWiro, rodesac alfa-adrenerguli blokerebi tamsulozinis CaTvliT miiReba PDE5 inhibitorebTan erTad. alfa-adrenerguli blokerebi da PDE5 inhibitorebi arian vazodilatatorebi, romlebic amcireben sisxlis wnevas. am ori jgufis preparatebis erTad gamoyenebam SeiZleba gamoiwvios simptomuri hipotenzia (ix. urTierTqmedebebi).

intraoperaciuli feradi garsis (iris) Cavardnis sindromi

intraoperaciuli **feradi garsis (iris) Cavardnis** sindromi (IFIS, patara gugis sindromis varianti) dafiqsirda kataraktas operaciis dros zogierT pacientSi, romlebic mkurnalobden alfa-1 adrenerguli blokerebiT, tamsulozinis CaTvliT. IFIS-ma SeiZleba gamoiwvios operaciis dros da Semdgom periodSi Tvalis mxriv garTulebebis zrda.

preoperaciuli Sefasebisas, kataraktas qirurgebma da ofTalmologebs gundma unda gaarkvios mkurnalobs an mkurnalobda Tu ara patienti duodartiT, raTa moxdes Sesabamisi zomebis miReba IFIS-ganviTarebis SemTxvevaSi.

tamsulozinis moxсна kataraktas operaciamede 1-2 kviriT adre miCneulia sasargeblad, magram kataraktas operaciamede Terapiis Sewyvetis sargebloba da xangrZlivoba jerjerobiT ar aris dadgenili..

gaJonvadi kafsulebi

dutasteridi Seiwoveba kanidan, aqedan gamomdinare qalebi da bavSvebi unda moeridon gaJonvad kafsulebTan kontakts. Tu adgili aqvs gaJonvad kafsulebTan kontakts, kontakts are unda daibanon dauyovnebliv sapniT da wyliT (ixile orsuloba da laqtacia).

CYP3A4 da CYP2D6-is inhibitorebi

tamsulozinis hidroqloridis CYP3A4-is Zlier inhibitorebTan (mag., ketokonazoli), an naklebad, CYP2D6-is Zlier inhibitorebTan (mag., paroqsetini) erTdroulma gamoyenebam SeiZleba gazardos tamsulozinis eqspozicia (ix. urTierTqmedebebi). aqedan gamomdinare tamsulozinis hidroqloridi rekomendebuli ar aris pacientebisTvis, romlebic iReben CYP3A4-is Zlier inhibitorebs da sifrTxilea saWiro pacientebSi, romlebic iReben CYP3A4-is saSualo siZlieris inhibitorebs (mag. eriTromicini), Zlier an sust CYP2D6-is inhibitorebs, orive CYP3A4-is da CYP2D6-is inhibitorebis kombinacias, an pacientebSi romlebSic cudad xdeba CYP2D6-is metabolizmi.

RviZlis funqciis darRveva

RviZlis funqciis darRvevis gavlena dutasteridis farmakokinetikaze Seswavlili ar aris. radgan dutasteridi farTod metabolizdeba da naxevardaSlis periodi Seadgens 3-5 kviras, sifrTxilea saWiro *duodartis* gamoyenebisas RviZlis daavadebis mqone pacientebSi (ix. dozireba da miRebis wesi da farmakokinetika).

urTierTqmedebebi

duodartis urTierTqmedebis kvlevebi ar Catarebula. Semdegi monacemebi moicavs individualur informacias.

dutasteridi

In vitro metabolizmis kvlevebi aCvenebs, rom dutasteridi metabolizdeba adamianis citoqrom P450 sistemis izoferment CYP3A4-iT. aqedan gamomdinare sisxliSi dutasteridis koncentracia SeiZleba gaizardos CYP3A4 inhibitorebis gamoyenebisas.

II fazis kvlevis monacemebma aCvena dutasteridis klirensis daqveiTeba CYP3A4 inhibitorebTan erTad gamoyenebisas, rogoricaa verapamili (37%) da dilTiazemi (44%). amis sawinaaRmdegod klirensis daqveiTeba ar aRiniSna, rodesac dutasteridTan erTad gamoiyeneboda amlodipini, kalciumis arxebis sxva antagonistebi. klirensis daqveiTeba da dutasteridis Semdgomi zemoqmedebis zrda CYP3A4-is inhibitorebis gamoyenebisas klinikurad naklebad mniSvnelovani iqneba usafrTxoebis farTo profilis gamo (pacientebSi gamoiyeneboda rekomendebul dozaze 10-er maRali doza 6 Tvis ganmavlobaSi). aqedan gamomdinare doza koreqcias ar saWiroebs.

In vitro dutasteridi ar metabolizdeba adamianis citoqrom P450 sistemis izofermentebiT - CYP1A2, CYP2A6, CYP2E1, CYP2C8, CYP2C9, CYP2C19, CYP2B6 da CYP2D6.

dutasteridi arc in vitro ainhibirebs adamianis citoqrom P450 wamlis metabolizmSi monawile fermentebis da arc in vivo aaqtiurebs citoqrom P450 izofermentebis CYP1A, CYP2B da CYP3A virTagvebsa da ZaRlebSi, acenokoumorolis, fenprokoumonis, diazepamis an fenitoinis Canacvlebas plazmis cilebidan, Tavis mxriv arc es modeluri SenaerTebi Caanacvleben dutasterids. nivTierebebi, romlebic Semowmebulia adamianSi wamalTSoris urTierTqmedebaze, moicavs tamsulozins, terazozins, varfarins, digoqsins da qolestiramins, da klinikurad mniSvnelovani farmakokinetikuri an farmakodinamikuri urTierTqmedeba ar gamovlenila.

miuxedavad imisa, rom ar Catarebula specifiuri kvlevebi sxva SenaerTebTan urTierTqmedebis Sesafaseblad, subieqtebis daaxloebiT 90% did III fazis kvlevaSi iRebda dutasterids sxva preparatebTan erTad. klinikur kvlevebSi dutasteridis gamoyenebisas antihyperlipidemiur saSualebebTan, angiotenzin gardamqmneli fermentis (agf) inhibitorebTan, beta-adrenergul blokerebTan, kalciumis arxebis blokerebTan, kortikosteroidebTan, SardmdenebTan, anTebis sawinaaRmdego arasteroidul preparatebTan, fosfodiesTerazas V tipis inhibitorebTan da qinolonis rigis antibiotikebTan erTad, ar aRiniSna klinikurad mniSvnelovani gverdiTi efeqtebi.

tamsulozini

arsebobs gazrdili hipotenziuri efeqtis Teoriuli riski, rodesac tamsulozini hidrolqoridi gamoiyeneba preparatebTan erTad, romlebmac SeiZleba Seamciros arteriuli wneva, saanesTezio saSualebebis, PDE5 inhibitorebis da sxva alfa-1 adrenerguli blokerebis CaTvliT. *duodarti* ar unda iqnas gamoyenebuli sxva alfa-1 adrenergul blokerebTan erTad.

tamsulozini hidroqloridis da ketokonazolis (CYP3A4-is Zlieri inhibitori) erTad gamoyenebam gamoiwvia tamsulozini C_{max} da AUC-s 2.2 da 2.8 punqtiT zrda, Sesabamisad. tamsulozini hidroqloridis da paroqsetini (CYP2D6-is Zlieri inhibitori) erTad gamoyenebam gamoiwvia tamsulozini hidroqloridis C_{max} da AUC-s zrda 1.3 da 1.6 punqtiT, Sesabamisad. moqmedebis msgavsi zrda CYP3A4-is Zlieri inhibitorTan erTad gamoyenebisas mosalodnelia CYP2D6 susti metabolizmis mqone pirebSi Zlieri metabolizmis mqone pirebTan SedarebiT. orive CYP3A4 da CYP2D6 inhibitorebis tamsulozini hidroqloridTan erTad gamoyenebis efeqtebi klinikurad ar aris Sefasebuli, Tumca arsebobs tamsulozini moqmedebis mniSvnelovnad gazrdis potenciali (*ix. gafrTxilebebi da usafrTxoebis zomebi*). tamsulozini hidroqloridis (0.4mg) da cimetidini (400mg 6 saatSi erTxel 6 dRis ganmavlobaSi) iwvevda klirensis daqveiTebas (26%) da tamsulozini hidroqloridis AUC (44%) zrdas. sifrTxilea saWiro *duodartis* cimetidinTan erTad gamoyenebisas.

tamsulozini hidroqloridis da varfarins Soris gansazRvruli wamalTSorisi urTierTqmedebis kvleva ar Catarebula. SezRuduli in vitro da in vivo kvlevebis SezRuduli monacemebi daskvnis gareSea. sifrTxilea saWiro varfarinis da tamsulozini hirolqoridis erTad gamoyenebisas.

sam kvlevaSi, sadac tamsulozini (0,4mg 7 dRis ganmavlobaSi, Semdeg 0,8mg 7 dRis ganmavlobaSi) gamoiyeneboda atenololTan, enalaprilTan an nifedipinTan erTad sami Tvis ganmavlobaSi urTierTqmedeba ar aRiniSna; aqedan gamomdinare dozis koreqcia saWiro ar aris rodesac es preparatebi gamoiyeneba *duodartTan* erTad.

tamsulozini hidroqloridis (0.4mg/dReSi ori dRis ganmavlobaSi, Semdeg 0.8mg/dReSi 5-8 dRis ganmavlobaSi) da Teofilinis erTjeradi intravenuri dozis (5mg/kg) gamoyenebam ar gamoiwvia cvlilebebi Teofilinis farmakokinetikaSi; aqedan gamomdinare dozis koreqcia saWiro ar aris.

tamsulozini hidroqloridis (0,8mg/dReSi) da furosemidis erTjeradi intravenuri dozis (20mg) erTad gamoyeneba iwvevs tamsulozini hidroqloridis Cmax da AUC-s 11 da 12 %-iT Semcirebas, Tumca es cvlilebebi klinikurad umniSvneloa da dozis koreqcia aucilebeli ar aris.

orsuloba da laqtacia

duodartis efeqtis gamosavlenad orsulobaze, laqtaciasa da fertilobaze kvlevebi ar Catarebula. Semdegi monacemebi miuTiTebis individualur SemTxvevebze.

fertiloba

dutasteridi

dutasteridis 0,5mg/dReSi dozis gavlena spermis maxasiaTeblebze Sefasda 18-52 wlis asakis janmrTel moxaliseebSi (n=27 dutasteridis, n=23 placebo) 52 kviriani mkurnalobis da mkurnalobis Semdgomi 24 kviriani dakvirvebis ganmavlobaSi. 52 kviraze spermis saerTo raodenobis, spermis moculobis da spermis moZraobis saSualo procentuli, Semcireba sawyis donesTan SedarebiT iyo Sesabamisad 23%, 26% da 18% dutasteridis jgufSi placebo jgufTan SedarebiT. spermis koncentracia da morfologia ucveli rCeboda. 24 kviriani dakvirvebis Semdeg spermis saerTo raodenobis saSualo procentuli cvlileba dutasteridis jgufSi rCeboda 23%-iT dabali sawyis donesTan SedarebiT. maSin rodesac spermis yvela parametris saSualo maCvenebeli drois yvela monakveTSi rCeboda normis farglebSi da ar Seesabameboda klinikuri mniSvnelobis cvlilebisTvis winaswar winaswar gansazRvrul kriteriumebis (30%), dutasteridis jgufSi or patients aReniSna spermis raodenobis daqveiTeba 90%-iT 52 kviraze nawilobriv gamojanmrTelebiT 24 kviriani dakvirvebis Semdeg. spermis maxasiaTeblebze dutasteridis gavlenis klinikuri mniSvneloba individualuri pacientebis fertilobisTvis ucnobia.

tamsulozini

spermis raodenobasa da funqciaze tamsulozini hidroqloridis efeqti Sefasebuli ar aris.

orsuloba

duodarti ukunaCvenebia qalebSi gamoyenebisTvis.

dutasteridi

dutasteridi Seswavlili ar aris qalebSi, radgan prelinikuri usafrTxoebis monacemebi miuTiTebis, rom dihidrotestosteronis mocirkulire donis supresia SeiZleba ainhibirebdes gareTa sasqeso organoebis ganviTarebas mamrobiTi sqesis nayofSi, romlis dedasac Sexeba hqonda dutasteridTan.

tamsulozini

tamsulozini hidroqloridis gamoyeneba orsul virTxebSi da kurdRlebSi Terapiulze maRali doziT ar iwvevda nayofis dazianebas.

laqtacia

duodarti ukunaCvenebia qalebSi gamoyenebisTvis.

ucnobia gamoiyofa Tu ara dutasteridi an tamsulozini dedis rZeSi.

gavlena avtomobilis marTvis da meqanizmebTan muSaobis unarze

ar Catarebula kvlevebi *duodartis* efeqtis Sesaswavlilad iseTi moqmedebebis Sesasruleblad, romlebic moiTxovs gansjis, motorul an SemecnebiT unar-Cvevebs. Tumca, pacientebi unda iyvnen informirebulebi orTostatul hipotenziasTan dakavSirebuli simptomebis Sesazlo gamovlenis Sesaxeb, rogoricav Tavbrusxveva *duodartis* miRebisas.

gverdiTi reaqciebi

ar Catarebula *duodartiT* klinikuri kvlevebi; Tumca kombinirebuli miRebis Sesaxeb informacia xelmisawvdomia CombAT (avodartis da tamsulozini kombinacia) kvlevaSi, sadac Seadares dutasteridis 0,5mg da tamsulozini 0,4mg erTxel dReSi gamoyeneba 4 wlis ganmavlobaSi, rogorc kombinirebuli an rogorc monoTerapiis saxiT.

agreTve mowodebulia informacia individualuri komponentebis (dutasteridi da tamsulozini) gverdiTi movlenebis Sesaxeb.

dutasteridis da tamsulozini erTad gamoyeneba**klinikuri kvlevebis monacemebi**

individualuri komponentebis gverdiTi reaqciebis Sesaxeb informacia (1% an meti kumulaciuri sixSire) aRwerilia CombATkvlevis dros.

gverdiTi reaqcia	sixSire mkurnalobis periodSi			
	1 weli	2 weli	3 weli	4 weli
kombinacia ^a (n)	(n=1610)	(n=1428)	(n=1283)	(n=1200)
dutasteridi	(n=1623)	(n=1464)	(n=1325)	(n=1200)
tamsulozini	(n=1611)	(n=1468)	(n=1281)	(n=1112)
impotencia, ^b				
kombinacia	6%	2%	<1%	<1%
dutasteridi	5%	2%	<1%	<1%
tamsulozini	3%	1%	<1%	<1%
Secvlili (daqveiTebuli) libido ^b				
kombinacia	5%	<1%	<1%	0%
dutasteridi	4%	1%	<1%	0%
tamsulozini	2%	<1%	<1%	<1%
eakulaciis darRvevebi ^b				
kombinacia	9%	1%	<1%	<1%
dutasteridi	1%	<1%	<1%	<1%
tamsulozini	3%	<1%	<1%	<1%
ZuZus daavadebebi ^c				

kombinacia	2%	<1%	<1%	<1%
dutasteridi	2%	1%	<1%	<1%
tamsulozini	<1%	<1%	<1%	0%
Tavbrusxveva				
kombinacia	1%	<1%	<1%	<1%
dutasteridi	<1%	<1%	<1%	<1%
tamsulozini	1%	<1%	<1%	<0%

- a) kombinacia=dutasteridi 0,5mg dReSi erTxel + tamsulozini 0,4mg dReSi erTxel.
- b) es sqesobrivi gverdiTi movlenebi dakavSirebulia dutasteridiT mkurnalobasTan (maT Soris monoTerapia da tamsulozinTan kombinacia). es gverdiTi movlenebi SeiZleba SenarCundes mkurnalobis Sewyvets Semdegac. dutasteridis roli am persistenciaSi ar aris cnobili
ZuZus mtkivneulobis da ZuZus zomis gazrdis CaTvliT

dutasteridiT monoTerapia

klinikuri kvlevis monacemebi

dutasteridis III fazian placebo kontrolirebad kvlevaSi (n=2167) placebosTan SedarebiT (n=2158), mkvlevarebis mier Sefasebuli preparatTan dakavSirebuli gverdiTi movlenebi erTi da or wliani mkurnalobis Semdeg iyo msgavsi tipis da sixSiris mixedviT cxrili zemoT).

gverdiTi movlenebis profilis cvlileba ar SeiniSneboda Semdgomi 2 wlis ganmavlobaSi am kvlevebis Ria gagrZelebis fazaSi.

postmarketinguli monacemebi

klinikuri kvlevebis monacemebidan miRebuli gverdiTi movlenebis garda, qvemoT CamoTvilia postmarketinguli gverdiTi reaqsiebi organoTa sistemis klasis da sixSiris mixedviT: sixSire gansazRvrulia rogorc: Zalian xSiri ($\geq 1/10$), xSiri ($\geq 1/100 - < 1/10$), araxSiri ($\geq 1/1000 - < 1/100$), iSviaTi ($\geq 1/10000 - < 1/1000$) da Zalian iSviaTi ($< 1/10000$) izolirebuli SemTxvevebis CaTvliT. post-marketinguli monacemebiT gansazRvruli sixSiris kategoriebi asaxavs aRweris aRweris angariSis maCvnebelis da ara namdvil sixSires. imunuri sistemis darRvevebi

Zalian iSviaTi: alergiuli reaqsiebi, gamonayaris, qavilis, urtikariis, lokalizebuli SeSupebis da angioedemis CaTvliT.

fsiqiatriuli darRvevebi

Zalian iSviaTi: depresiuli ganwyoba

kanis da kanqveSa qsovilis darRvevebi

iSviaTi: alopecia (upiratesad sxელის Tmis cvena), hipertriozi

reproduqciuli sistemis da ZuZus mxriv darRvevebi

Zalian iSviaTi: saTesleebis tkivili da SeSupeba.

tamsulozinis monoTerapia

klinikuri kvlevis monacemebi da postmarketinguli monacemebi

GSK ar flobs usafrTxoebis monacemTa bazas romelime erTi Semadgenlobis tamsulozinis produqtisTvis; amitom qvemoT moyvanili gverdiTi reaqciebi da sixSiris kategoriebi efuzneba gamoqveynebul monacemebs. qvemoT mocemul cxrilSi, xSiri da araxSiri reaqciebi Seesabameba klinikur kvleebSi dafiqsirebul maCveneblebs da sixSiris kategoriebi Cveulebriv asaxavs placebos sixSires. iSviaTi da Zalian iSviaTi reaqciebi Seesabameba posmarketinguli angariSebidan gamovlenil movlenebs da sixSiris kategoriebi asaxavs angariSebis maCveneblebs.

organoTa sistemis klasi	sixSiris kategoria			
	xSiri ($\geq 1/100$ <1/10)	araxSiri ($\geq 1/1000$ <1/100)	iSviaTi ($\geq 1/10000$ <1/1000)	Zalian iSviaTi (<1/10 000) izolirebuli SemTxvevebis CaTvliT
gulis darRvevebi		palpitacia		
gastro-intestinuri darRvevebi		Sekruloba dairea Rebineba		
zogadi darRvevebi da Seyvanis adgilis darRvevebi		asTenia		
nervuli sistemis darRvevebi	Tavbrusxveva		sinkope	
reproduqciuli sistemis da ZuZus darRvevebi	aranormaluri eakulacia			priapizmi
respiratoruli, Torakaluri da mediastinaluri darRvevebi		riniti		
imunuri sistemis darRvevebi		gamonayari, qavili, urtikaria	angioedema	stivens-jonsonis sindromi
sisxlZarRvovani darRvevebi		posturaluri hipotenzia		

post-marketinguli dakvirvebebis dros, kataraqtas operaciis dros intraoperaciuli feradi garsis (iris) Cavardnis sindromis (IFIS), patara gugis sindromis variantis Sesaxeb cnobebi asocierebulia alfa-1 adrenerguli blokerebiT TerapiasTan; tamsulozinis CaTvliT (ix. gafrTxilebebi da usafrTxoebis zomebi).

post-marketinguli gamocdileba: garda amisa, tamsulozinis gamoyenebasTan dakavSirebulia winagulebis fibrilacia, ariTmia, taqikardia, qoSini, epistaqsisi, mxedvelobis dabindva, mxedvelobis gauareseba, multiformuli eriTema, eqsfoliaciuri dermatiti da piris simSrale.

Warbi dozireba

duodartis dozis gadaWarbebis Sesaxeb monacemebi ar arsebobs. Semdegi debulebebi asaxavs calkeul komponentebze arsebul informacias.

dutasteridi

moxaliseTa kvleebSi dutasteridis erTjeradi doz 40mg/dReSi (80-jer aRemateba Terapiul dozas) 7 dRis ganmavlobaSi gamoiyeneboda usafrTxoebis mniSvnelovani darRvevebis gareSe. klinikur kvleebSi 5mg/dReSi dozebi yoveldRiurad gamoiyeneboda pacientebSi 6 Tvis ganmavlobaSi, damatebiTi gverdiTi efeqtebi ar gamovlinda 0.5mg dozirebis SemTxvevaSi.

specifiuri antidoti dutasteridisTvis ar arsebobs, amitom Warbi dozirebis SemTxvevaSi saWiroa saTanado simptomuri da SemanarCunebeli Terapiis Catareba.

tamsulozini

tamsulozinis hidroqloridis dozis gadaWarbebis Sedegad ganviTarebuli mwvave hipotenziis SemTxvevaSi saWiroa kardio-vaskularuli mxardaWera. sixxlis wnevis aRdgena da gulis riTmis normalizeba SeiZleba ganxorcieldes avadmyofis dawveniT. Tu es arasakmarisia, maSin unda moxdes moculobis gamafarToeblebis da aucileblobis SemTxvevaSi vazopresorebis gamoyeneba da saWiroebis SemTxvevaSi Tirkmlis funqciis monitoringi. laboratoriuili gamokvlevebi miuTiTebis, rom tamsulozinis hidrolqoridi 94%-99%-iT ukavSirdeba plazmis cilebs; aqedan gamomdinare misi gamoyofisTvis dializi ar iqneba sasargeblo.

farmakologiuri maxasiaTeblebi

farmakodinamika

duodarti aris ori preparatis kombinacia moqmedebis damatebiTi meqanizmiT, romelic aumjobesebs simptomებს prostatitis keTilTvisebiani hiperplaziis mqone pacientebSi (BPH): dutasteridi, 5 alfa-reduqtazas (5 ARI) ormagi inhibitori da tamsulozinis hidroqloridi, alfa-1a-adrenoreceptorebis antagonisti.

duodartis, rogorc fiqsirebuli dozis kombinaciis farmakodinamika ar unda gansxvavdebodes dutasteridisa da tamsulozinis farmakodinamikisgan, romlebic erToblivad miiReba calkeuli komponentebis saxiT.

dutasteridi

dutasteridi warmoadgens 5 alfa-reduqtazas ormag inhibitors. is ainhibirebs orives 1 tipis da 2, 5 tipis alfa-reduqtazas izofermentebis romlebic pasuxismgeblebi arian testosterinis 5 alfa-dihydrotestosteronad gardaqmnaze (DHT), DHT aris androgeni,romelic ZiriTadad pasuxismgebelia prostatitis jirkvlovani qsovilis hiperplaziase.

dutasteridi amcirebs DHT-s dones, amcirebs prostatitis moculobas, aumjobesebs qvemo saSarde traqtis simptomებს da Sardis nakads da amcirebs AUR da BPH-sTan dakavSirebuli qirurgiuli Carevis risks.

dutasteridis dRiuri dozebis maqsimaluri efeqti DHT-s Semicirebaze doza-damokidebulia da aRiniSneba 1-2 kviraSi. dutasteridis 0,5mg dRiuri dozirebis 1 da 2 kviris Semdeg, SratSi DHT-s saSualo koncentracia Semcirca 85 da 90%-iT Sesabamisad.

BPH pacientebSi, romlebsac mkurnalobdnen 0.5mg dutasteridiT dReSi, DHT-s done saSualod mcirdeboda 94%-iT 1 wlis Semdeg da 93% 2 wlis Semdeg, SratSi testosteronis saSualo zrda iyo 19%. es aris 5 alfa-reduqtazas inhibitorebis mosalodneli efeqti da ar iwvevs raime gverdiT movlenas.

tamsulozini

tamsulozini ainhibirebs alfa-1a adrenergul receptorebs prostatitis stromis gluv kunTebSi da Sardis buStis yeSi. prostatitis α 1-receptorebis daaxloebiT 75% aris α 1a qvetipis.

tamsulozini zrdis Sardis maqsimalur nakads prostatisa da ureTris gluvi kunTebis daWimulobis SemicirebiT, riTac xsnis obstruqcias. is agreTve xnis gaRizianebs da obstruqciis simptomებს kompleqss, romlebsic Sardis buStis arastabiluroba da qvemo saSarde traqtis gluvi kunTebis daWimuloba mniSvnelovan rols TamaSobs. alfa-1 adrenergulma blokerebma SeiZleba Seamciros sixxlis wneva periferiuli winaarMdegobis daqveiTebiT.

farmakokinetika

bioeqivalentoba gamovlinda dutasteridi-tamsulozinis da calke dutasteridis da tamsulozinis kafsulebis dozirebisas.

erTjeradi dozebis bioeqivalentobis kvleva Catarda uzmoze da naWam mdgomareobaSi. dutasterid-tamsulozinSi aRiniSna tamsulozinis komponentis C_{max}-s 30% Semcireba sakvebis miRebis Semdeg uzmo mdgomareobasTan SedarebiT. sakvebi gavlenas ar axdenda tamsulozinis AUC-ze.

Sewova

dutasteridi

dutasteridi miiReba peroralurad xsnari rbili Jelatinis kafsulis saxiT. erTjeradi 0,5mg dozis miRebis Semdeg plazmaSi dutasteridis plazmuri koncentracia miiRweva 1-3 saaTSi. mamakacebSi absoluturi bioSeRwevadoba Seadgens daaxloebiT 60%-s 2 saaTiani intravenuri infuziis Semdeg. dutasteridis bioSeRwevadobaze sakvebi ar moqmedebs.

tamsulozini

tamsulozinis hidrolqoridi Seiwoveba nawlavidan da TiTqmis srulad bioSeRwevadia. tamsulozinis hidroqloridi avlens xazovan kinetikas, erTjeradi da mravaljeradi dozirebis Semdeg, stabiluri koncentracia miiRweva dReSi erTxel dozirebidan me-5 dRes. tamsulozinis hidroqloridis Sewovis siswrafe mcirdeba sakvebis miRebiT. patients SeuZlia xeli Seuwyos Sewovis erTgvarovnebas, romelic tamsulozinis hidroqlorids yovelTvis iRebes sakvebis miRebidan 30 wuTis Semdeg dRis erTsa da imave dros.

ganawileba

dutasteridi

farmakokinetikurma monacemebma erTjeradi da ganmeorebiTi peroraluri dozebis Semdeg aCvena, rom dutasterids gaaCnia farTo ganawilebis moculoba (300-500 l). dutasteridi farTod ukavSirdeba plazmis cilebs (>99.5%). dRiuri dozirebis Semdeg SratSi dutasteridis koncentracia aRwevs stabiluri mdgomareobis koncentraciis 65%-s 1 Tvis Semdeg da daaxloebiT 90%-s 3 Tvis Semdeg. stabiluri mdgomareobis koncentracia SratSi (C_{ss}) daaxloebiT 40ng/ml miiRweva 0.5 mg/dReSi erTxel miRebiT 6 Tvis Semdeg. SratIs msgavsad, spermaSi dutasteridis koncentracia stabilur mdgomareobas aRwevs 6 TveSi. 52 kviriani mkurnalobis Semdeg spermaSi dutasteridis koncentracia Seadgenda saSualod 3.4 nanogrami/ml-s (0.4-14ng/ml). dutasteridis moxvedra Sratidan spermaSi Seadgens daaxloebiT 11.5%-s.

tamsulozini

tamsulozinis hidroqloridis ganawilebis saSualo stabiluri mdgomareobis moculoba intravenuri miRebis Semdeg 10 janmrTel mamakacSi iyo 16 l, rac Seefereba organizmis ujredSorIs siTxeebSi ganawilebas. tamsulozinis hidroqloridi farTod ukavSirdeba adamianis plazmis cilebs (94% - 99%), ZiriTadad alfa-1 mJava glikoproteins (AAG), xazovani kavSiriT koncentraciis farTo diapazonSi (20 - 600 nanogrami/ml).

biotransformacia

dutasteridi

In vitro, dutasteridi metabolizdeba adamianis citoqrom P₄₅₀ izofermentiT CYP3A4 or mcire monohidroqsilirebul metabolitad, magram is ar metabolizdeba CYP1A2, CYP2A6, CYP2E1, CYP2C8, CYP2C9, CYP2C19, CYP2B6 an CYP2D6 mier.

adamianis SratSi dozirebis Semdeg stabiluri mdgomareobis miRwevisas, masiuri speqtrometriiT aRmoCenilia ucveleli dutasteridi da 3 ZiriTadi metaboliti (4'-hidroqsidutasteridi, 1,2-dihidroductasteridi da 6-hidroqsidutasteridi) da 2 mcire metaboliti (6,4'-dihidroqsidutasteridi da 15-hidroqsidutasteridi). dutasteridis adamianis SratIs 5 metaboliti aRmoCenilia virTxebis SratSi, Tumca hidroqsilis danamatebis stereooqimia 6 da 15 poziciaze adamianis da virTxebis metabolismSi ar aris cnobili.

tamsulozini

ar aRiniSneba enanTiomeruli biotransformacia tamsulozinis hidroqloridis [R(-) izomerisa] S(+) izomerad adamianebsi. tamsulozinis hidroqloridi intensiurad metabolizdeba RviZiSi citoqrom P₄₅₀ fermentiT da dozis 10%-ze naklebi SardSi gamoiyofa ucveleli saxiT, Tumca, adamianSi metabolitebis farmakokinetikuri

profili dadgenili ar aris. In vitro Sedegebi miuTiTebS, rom CYP3A4 da CYP2D6 monawileoben tamsulozinis metabolizmSi, iseve rogorc sxva CYP izofermentebis umniSvnelo monawileobas. RviZiSi prepratebis metabolizmSi monawile izofermentebis inhibirebam SeiZleba gamoiwvios tamsulozinis efeqtis gazrda (ix. *gafrTxilebebi da sifrTxilis zomebi da urTierTqmedebebi*).

tamsulozinis hidroqloridis metabolitebi gadian intensiur koniugacias glukuronidTan an sulfatTan TirkmliT eqskreciamde.

eliminacia

dutasteridi

dutasteridi intesniurad metabolizdeba. dutasteridis dReSi 0,5 mg/dReSi peroraluri dozirebis Semdeg stabilur mdgomareobamde adamianebSi miRebuli dozis 1.0% - 15.4% (saSualod 5,4%) gamoiyofa rogorc dutasteridi ganavalTan erTad. danarCeni gamoiyofa ganavalTan erTad 4 didi metabolitis saxiT 39%, 21%, 7% da 7% da 6 mcire metaboliti (TiToeuli 5%-ze naklebi).

adamianis SardSi aRmoCenilia uc vleli dutasteridis mxolod narCeni raodenoba (0.1%-ze naklebi).

Terapiul koncentraciebSi, dutasteridis naxevardaSlis periodi Seadgens 3-5 kviras.

SratSi koncentracia rCeba aRmoCenadi (0.1 nanogrami/ml-ze meti) mkurnalobis moxsnidan 4-6 Tvis ganmavlobaSi.

SratSi dabali koncentraciebiT (3 nanogrami/ml-ze naklebi), dutasteridi swrafad gamoiyofa koncentracia-damokidebuli da koncentracia-damoukidebeli gzebiT. 5 mg an naklebi erTjeradi dozis miRebisas aRiniSna swrafi klirensi da mokle naxevardaSlis periodi 3-9 dRe.

SratSi 3 nanogrami/ml-ze maRali koncentraciis dros dutasteridi nela gamoiyofa (0.35-dan 0.58 l/sT-mde), ZiriTadad, xazovan, aragajerebuli eliminaciis gziT, terminaluri naxevardaSlis periodiT 3-dan 5 kviramde. Terapiuli koncentraciebiT, 0.5 mg/dReSi ganmeorebiTi dozirebis Semdeg dominirebs ufro neli klirensi da saerTo klirensi aris xazovani da koncentracia-damoukidebuli.

tamsulozini

tamsulozinis naxevardaSlis periodi 5-7 saaTs Seadgens. daaxloebiT 10% gamoiyofa uc vleli saxiT SardSi.

xandazmulebi

dutasteridi

dutasteridis farmakokinetika da farmakodinamika Sefasda 24-87 wlis asakis 36 janmrTel mamrobiTi sqesis subieqtSi dutasteridis erTjeradi 5 mg dozis miRebis Semdeg. dutasteridis efeqti, warmodgenili AUC da Cmax monacemebiT, statistikurad ar gansxvavdeboda asakobrivi jgufebis Sedarebisas. naxevardaSlis periodi statistikurad ar gansxvavdeboda 50-69 wlis jgufis 70 welze ufrosi asakis jgufebTan Sedarebisas, romlebic ZiriTadad moicavs prostatitis keTilTvisebiani hiperplaziis mqone (BHP) pirebs. aranairi gansxvaveba preparatis efeqtSi, romelic izomeba BHP donis SemcirebiT, ar dafiqsirebula asakobrivi jgufebis Soris. Sedegebma aCvena, rom asakis mixedviT dutasteridis dozis koreqcia saWiro ar aris.

tamsulozini

tamsulozinis hidroqloridis saerTo eqspoziciis (AUC) da naxevar-daSlis periodis jvaredini kvleva aCvenebs, rom tamsulozinis hidrolqoridis farmakokinetikuri ganawileba SeiZleba odnav gaxangrZlivdes xandazmul mamakacebSi axalgazrda, janmrTel mamrobiTi sqesis moxaliseebTan SedarebiT. klirensi ar aris damokidebuli tamsulozinis hidroqloridis AAG-sTan kavSirisgan, magram qveiTdeba asakTan erTad, iwvevs 40%-iT ufro maRal eqspozicias 55-75 wlis subieqtebSi 20-32 wlis pirebTan SedarebiT.

Tirkmlis funqciis darRveva

dutasteridi

dutasteridis farmakokinetikaze Tirkmlis dazianebis efeqti Seswavlili ar aris. Tumca adamianis SardSi isazRvreba 0.5mg dozis myari mdgomareobis 0.1%-ze naklebi, aqedan gamomdinare Tirkmlis dazianebisas dozis cvlileba aucilebeli ar aris.

tamsulozini

tamsulozinis hidroqloridis farmakokinetika Seadares 6 subieqtSi, romlebsac aReniSnebodaT msubuqisaSualo ($kk \leq 30 \text{ml/wT} < 70 \text{ml/wT} \cdot 1.73 \text{m}^2$) saSualo-mZime ($kk \leq 10 \text{ml} < 30 \text{ml/wT} \cdot 1.73 \text{m}^2$) xarixsis Tirkmlis dazianebe da 6 janmrTel subieqtSi ($kk > 90 \text{ml/wT} \cdot 1.73 \text{m}^2$). aRiniSna tamsulozinis plazmuri koncentraciis cvlileba AAG-sTan dakavSirebis Secvlis gamo tamsulozinis SeukavSirebeli (aqtiuri) koncentracia da klirensi met naklebad mudmivi darCa. aqedan gamomdinare Tirkmlis dazianebis mqone pacientebSi saWiro ar aris tamsulozinis hidroloqridis tabletebis dozirebis cvlileba. Tumca pacientebi Tirkmlis daavadebis bolo stadiiT ($kk < 10 \text{ml/wT} \cdot 1.73 \text{m}^2$) Seswavlili ar aris.

RviZlis funqciis darRveva

dutasteridi

dutasteridis farmakokinetikis efeqtebi RviZlis funqciis dazianebisas Seswavlili ar aris. (ix. gafrTxilebebi da usafrTxoebis zomebi). radgan dutasteridi eqstensiurad metabolizdeba eqspozicia SeiZleba ufro maRali iyos RviZlis funqciis dazianebis mqone pacientebSi.

tamsulozini

tamsulozinis hidrolqoridis farmakokinetika Seadares 8 subieqtSi RviZlis zomieri dazianebiT (Caild plus klasifikaciIT a da b xarixsi) da 8 janmrTel subieqtSi. aRiniSna tamsulozinis plazmuri koncentraciis cvlileba AAG -sTan dakavSirebis Secvlis gamo, magram SeukavSirebeli (aqtiuri) koncentracia mniSvnelovnad ar icvleba, mcired (32%) icvleba SeukavSirebeli tamsulozinis hidroqloridis klirensi. aqedan gamomdinare pacientebSi RviZlis zomieri dazianebiT aucilebeli ar aris tamsulozinis hidroqloridis dozis cvlileba. tamsulozinis hidroqloridi Seswavlili ar aris pacientebSi RviZlis mwvave dazianebiT.

klidikuri kvlevebi

Semdegi monacemebi asaxavs xelmisawvdom informacias dutasteridis da tamsulozinis Sesaxeb, calcalke an erTad gamoyenebisas.

avodarti 0.5mg dReSi, tamsulozini 0.4 mg/dReSi an *avodarti* 0.5 mg-s da tamsulozinis 0.4mg-s erTad gamoyeneba Sefasda 4844 mamrobiTi sqesis subieqtSi, romlebsac aReniSnebodaT prostatitis gadideba (30cc an meti), mravalcentrul, ormagad brma, paraleluri jgufebis kvlevaSi 4 wlis ganmavlobaSi.

pirveladi efeqturobis saboloo wertili 2 wliani mkurnalobisTvis iyo sawyisi donis gaumjobeseba prostatitis saerTaSoriso simptomebis SkaliT (IPSS). dutasteridis da tamsulozinis kombinacia ganapirobebs simptomebis ukeTes gaumjobesebas, vidre calkeuli komponentebi. 2 wliani mkurnalobis Semdeg, kombinirebulma mkurnalobam aCvena statistikurad mniSvnelovani simptomebis Skalis Secvlili saSualo gaumjobeseba -6.2 erTeuli sawyisi mdgomareobidan. simptomebis Skalis Secvlili saSualo gaumjobeseba individualuri Terapiisas iyo - 4.9 erTeuli *avodartisTvis* da - 4.3 erTeuli tamsulozinisTvis.

nakadis siswrafis Secvlili gaumjobeseba iyo 2.4ml/wamSi kombinaciisTvis, 1.9ml/wamSi *avodartisTvis* da 0.9ml/wamSi tamsulozinisTvis. BPH gavlenis indeqsis (BII) Secvlili saSualo gaumjobeseba iyo - 2.1 erTeuli kombinaciisTvis, -1.7 *avodartisTvis* da -1.5 tamsulozinisTvis. nakadis siswrafis da BII gaumjobeseba statistikurad mniSvnelovani iyo kombinirebuli TerapiisTvis orive monoTerapiasTan SedarebiT.

prostatitis saerTo moculobis da gardamavali zonis moculobis Semcireba mkurnalobis 2 wlis Semdeg iyo statistikurad mniSvnelovani kombinaciis gamoyenebisas tamsulozinis monoTerapiasTan SedarebiT.

pirveladi efeqturobis saboloo wertili mkurnalobis 4 wlisTvis iyo dro AUR-s an BPH-Tan dakavSirebuli operaciis pirveli movlenis dros. 4 wliani mkurnalobis Semdeg, kombinirebulma Terapiam mniSvnelovnad Seamcira AUR-s an BPH-Tan dakavSirebuli operaciis riski (65.8% riskis Semcireba $P < 0.001$ [95% CI

54.7%-74.1%] tamsulozinis monoTerapiasTan SedarebiT. 4 wliisTvis AUR–s an BPH-Tan dakavSirebuli operaciis sixSire iyo 4.2% kombinirebulis TerapiisTvis da 11.9% tamsulozinisTvis ($P<0.001$). *avodartiT* monoTerapiasTan SedarebiT, kombinirebulma Terapiam Seamcira AUR–s an BPH-Tan dakavSirebuli operaciis riski 19.6%-iT; gansxvaveba samkurnalo jgufebis Soris ar iyo mniSvnelovani ($P=0.18$ [95% CI-10,9%-41.7]). 4 wliisTvis AUR–s an BPH-Tan dakavSirebuli operaciis sixSire iyo 4.2% kombinirebuli TerapiisTvis da 5.2% *avodartisTvis*.

klinikuri progresi ganisazRvra rogorc simptomebis gauaresebis kompoziti, (IPSS), AUR–is BPH-Tan dakavSirebuli movlenebi, SeuTavsebloba, UTI, da Tirkmlis ukmarisoba. kombinirebuli Terapia dakavSirebuli iyo klinikuri progresirebis statistikurad mniSvnelovnad dabal sixSiresTan tamsulozinTan SedarebiT ($P<0.001$, 44.1% riskis Semcireba [95% CI-33.6%-53.0%]) 4 wliis Semdeg. klinikuri progresirebis sixSire kombinirebuli TerapiisTvis, tamsulozinisTvis da *avodartisTvis* iyo: 12.6, 21.5, 17.8% Sesabamisad.

statistikurad mniSvnelovani simptomebis Skalis Secvlili saSualo gaumjobeseba (IPSS) sawyisi mdgomareobidan iyo SenarCunebuli 2-idan 4 wlamde. simptomebis Skalis Secvlili saSualo gaumjobeseba iyo -6.3 erTeuli kombinirebuli TerapiisTvis, -5.3 erTeuli *avodartiT* monoTerapiisTvis da - 3.8 erTeuli tamsuloziniT monoTerapiisTvis. 4 wliani mkurnalobis Semdeg, nakadis siswrafis saSualo gaumjobeseba (Q_{max}) sawyisi mdgomareobidan iyo 2.4ml/wamSi kombinirebuli TerapiisTvis, 2.0ml/wm *avodartiT* monoTerapiisTvis da 0.7ml/wm tamsuloziniT monoTerapiisTvis. tamsulozinTan SedarebiT Q_{max} Secvlili saSualo gaumjobeseba sawyisi mdgomareobidan statistikurad mniSvnelovnad ufro maRali iyo kombinirebuli Terapiisas 6 Tviani Sefasebebisas 6-dan 48 Tvemde ($P<0.001$). *avodartTan* SedarebiT Q_{max} Secvlili saSualo gaumjobeseba sawyisi mdgomareobidan statistikurad mniSvnelovnad ar gansxvavdeboda kombinirebuli Terapiisgan ($P=0.050$ 48 Tves).

kombinirebuli Terapia mniSvnelovnad aRemateboda ($P<0.001$) tamsuloziniT monoTerapias da *avodartiT* monoTerapias janmrTelobis Sedegis parametrebis gaumjobesebaSi BII da BPH-Tan dakavSirebuli janmrTelobis statusi (BHS) meoTxe wliisTvis. BII-sTvis Secvlili saSualo gaumjobeseba sawyis mdgomareobidan iyo -2.2 erTeuli kombinaciisTvis, -1.8 *avodartisTvis* da -1.2 tamsulozinisTvis. BHS Secvlili saSualo gaumjobeseba sawyisi mdgomareobidan iyo -1.5 erTeuli kombinaciisTvis -1.3 *avodartisTvis* da -1.1 tamsulozinisTvis. 4-wliani mkurnalobis Semdeg prostatitis saerTo moculobis Semcireba da gardamavali zonis moculobis Semcireba statistikurad mniSvnelovani iyo kombinirebuli TerapiisTvis tamsuloziniT monoTerapiasTan SedarebiT.

dutasteridi

dutasteridi 0.5 mg/dReSi an placebo Seafases 4325 mamrobiTi sqesis pirebSi gadidebuli prostatitiT (30sm-ze didi), wina sam efeqtur 2 wlian multicentruL, placebo kontrolirebul, ormag brma kvlevaSi.

mamakacebSi prostatitis keTilTvisebiani hiperplaziiT (BHP), dutasetridi mkurnalobis da xel uSlis daavadebis progresirebas, orive riskis SemcirebiT, (Sardis mwvave Sekavebis) AUR da qirurgiuli Carevis saWiroebis riskis SemcirebiT da qveda saSarde traqtis simptomebis (LUTS), Sardis nakadis maqsimaluri siCqaris (Q_{max}) da prostatitis moculobis statistikurad mniSvnelovani gaumjobesebis uzrunvelyofiT placeboTan SefardebiT. qveda saSarde traqtis simptomebis (LUTS), Q_{max} da prostatitis moculobis gaumjobeseba dafiqsirda 24 Tvis ganmavlobaSi, da LUTS da Q_{max} gaumjobeseba gagrZelda momdevno 2 wliis ganmavlobaSi Ria gafarToebul kvlevebSi. Ggarda amisa, prostatitis moculobis Semcireba SenarCunda Semdegi 2 wliis ganmavlobaSi Ria gafarToebul kvlevebSi.

gulis ukmarisoba

4 wlian SedarebiT kvlevaSi *avodartis* tamsulozinTan erTad daniSvnisas da *avodarti* an tamsuloziniT monoTerapiisas mamakacebSi prostatitis keTilTvisebiani hiperplaziiT (BPH) (CombAT kvleva), kombinirebuli Terapiis jgufSi gulis ukmarisobis sixSire (14/1610, 0.9%) ufro maRali iyo, vidre monoTerapiis romelime jgufSi: *avodarti*, 4/1623 (0.2%) da tamsulozini, 10/1611, (0.6%). SedarebiTi riskis

Sefaseba gulis ukmarisobis pirveli epizodis gamovlenamde droisTvis Seadgenda 3.57 [95% CI 1.17, 10.8] kombinirebuli mkurnalobisTvis *avodarti*T monoTerapiasTan SedarebiT da 1.36 [95% CI 0.61, 3.07] tamsuloziniT monoTerapiasTan SedarebiT. 4 wliani qimioprevenciisas, placebos da dutasteridis gamoyeneba 50-75 wlis 8231 mamakacebSi prostatitis kibos winaswari uaryofiTis biofsiiT da sabaziso PSA maCvenebliT, romelic meryeobda 2.5-10 ng/ml-s Soris (REDUCE kvleva), gulis ukmarisobis sixSire ufro maRali iyo subieqtSi, romlebic iRebden *avodarts* (30/4105, 0.7%) placebosTan SedarebiT (16/4126, 0.4%) savaraudo SedarebiTi riski 1.91 [95% CI 1.04, 3.50] gulis ukmarisobis pirveli SemTxvevis gamosavlenad saWiro droisTvis. alfa-blokeris erTdrouli gamoyenebisas post-hoc analizSi gulis ukmarisobis sixSire ufro maRali iyo subieqtSi, romlebic iRebden *avodarts* da alfa blokereb erTdroulad (12/1152, 1.0%), im pirebTan SedarebiT, romlebic erTdroulad ar iRebden dutasteridis da alfa blokereb: *avodarti* alfa blokereb gareSe (18/2953, 0.6%), placebo da alfa blokereb (1/1399, <0.1%), placebo alfa blokereb gareSe (15/2727, 0.6%). dutasteridis (marto an alfa blokerebTan kombinaciaSi) da gulis ukmarisobas Soris kavSiri dadgenili ar aris (*ix. gafrTxilebebi da usafrTxoebis zomebi*).

prostatitis kibo da maRali xarisxis simsi vneebi

4 wlian placebos da *avodartis* SedarebiT kvlevaSi, romelic Catarda 50-75 wlis 8231 mamakacSi, prostatitis kibos winaswari uaryofiTis biofsiiT da sabaziso PSA-s maCvenebliT 2.5-10 ng/ml-s Soris (REDUCE kvleva), 6,706 subieqtSi xelmisawvdomi iyo prostatitis biofsiis monacemebi glisonis Skalis gansazRvrisTvis. kvlevaSi 1517 subieqtSi daesva prostatitis kibos diagnozi. mkurnalobis orive jgufSi biofsiiT aRmoCenili prostatitis kibos umravlesoba iyo dabali xarisxis (glisoni 5-6). ar aRiniSna gansxvaveba glisoni 7-10 xarisxis kibos sixSires Soris (p=0.81).

glisoni 8-10 xarisxis prostatitis kibos sixSire ufro maRali iyo *avodartis* jgufSi (n=29, 0.9%) placebos jgufTan SedarebiT (n=19, 0.6%) (p=0.15). 1-2 weliSi, glisoni 8-10 xarisxis kiboTi daavadebuli subieqtSi raodenoba msgavsi iyo *avodartis* (n=17, 0.5%) da placebos jgufSi (n=18, 0.5%). 3-4 weliSi, glisoni 8-10 xarisxis kibos diagnozi ufro meti raodenobis diagnozi daisva *avodartis* jgufSi (n=12, 0.5%) placebos jgufTan SedarebiT (n=1, <0.1%) (p=0.0035). ar arsebobs monacemebi dutasteridis efeqtis gansazRvrisTvis 4 wlis Semdeg mamakacebSi, romlebsac aReniSnebaT prostatitis kibos riski. glisoni 8-10 xarisxis kiboTi daavadebuli subieqtSi procentuli raodenoba Tanmimdevruli iyo kvlevis drois periodebSi (1-2 da 3-4 weli) *avodartis* jgufSi (0.5% drois yovel periodebSi), xolo placebos jgufSi glisoni 8-10 xarisxis kiboTi daavadebuli subieqtSi procentuli raodenoba ufro dabali iyo me-3-4 weli vidre 1-2 wlis ganmavlobaSi (<0.1% vs 0.5%, Sesabamisad). 4 wlian BPH kvlevaSi (CombAT), sadac biofsia protokolIT ar tardeboda da prostatitis kibos yvela diagnozi dafuznebuli iyo mizezobrivi biofsiaze, glisoni 8-10 xarisxis kibos sixSire iyo (n=8, 0.5%) *avodartis*Tvis, (n=11, 0.7%) tamsuloziniTvis da (n=5, 0.3%) kombinirebuli TerapiiTvis (*ix. gafrTxilebebi da usafrTxoebis zomebi*).

epidemiologiuri, populaciaze-dafuznebuli kvlevis (n=174.895) Sedegebma aCvena, rom 5-ARI gamoyeneba BHP/LUTS samkurnalod ar aris dakavSirebuli prostatitis kiboTi sikvdilianobis gazrdil riskTan (riskis koeficienti romelic daregulirebulia konkurenti riskebisTvis: 0.85, 95% CI 0.72, 1.01), rodesac xdeboda misi Sedareba alfa-blokerebis gamoyenebasTan. msgavsi Sedegebi aRiniSna prostatitis kiboTi daavadebuli mamakacebis epidemiologiur kvlevaSi (n=13.892) did britaneTSi (prostatitis kiboTi sikvdilianobis riskis koeficienti 5-ARI momxmareblebisTvis ara-momxmareblebTan SedarebiT: 0.86, 95% CI 0.69, 1.06). prospektulma kohortulma kvlevam "jandacvis profesionalis Semdgomi kvleva" (n=38.058), aseve aRmoaCina rom 5-ARI ar asocirdeba fatalur prostatitis kibosTan (riskis koeficienti: 0.99, 95%CI 0.58, 1.69).

zegavlina prostatitis specifiku antigenze (PSA) da prostatitis kibos gamovlinebaze

REDUCE kvlevaSi, pacientebSi, romlebsac hqondaT prostatitis kibos negatiuri biofsiis pasuxi da sawyisi PSA 2.5-10 ng/ml *avodarti*T mkurnalobam gamoiwvia Sratis saSualo PSA Semcireba daaxloebiT 50% mkurnalobidan 6 Tvis Semdeg maRali variabelobiT (standartuli gadaxra 30%) pacientebS Soris. PSA

supresia, romelic aRiniSna me-6 Tveze msgavsi iyo im mamakacebSi, visac ganuviTarda an ar ganuviTarda biofsiiT gamovlenili prostatitis kibo kvlevis dros (*ixile specialuri sifrTxilis zomebi*).

ZuZus kibos sixSire

BHP monoTerapiis klinikur kvlebebSi, romelic uzrunvelyofs *avodartiT* wlebis ganmavlobaSi namkurnaleb 3374 pacients, gamovlinda mamakacebis ZuZus kibos 2 SemTxveva *avodartiT* namkurnaleb pacientebSi, erTi 10 kviris Semdeg da erTi 11 Tvis Semdeg da 1 SemTxveva im pacientebS Soris, romlebic iRebden placebos. BHP Semdgom klinikur kvlebebSi da 50-75 wlis asakis 8231 mamakaci prostatitis kibos winaswari uaryofiti biofsiiT da sawyisi PSA 2.5-10.0ng/ml, rac uzrunvelyofs 17489 pacients *avodartis zemoqmedebiT* da 5027 pacients *avodartis* da tamsulozinis kombinaciis zemoqmedebiT wlebis ganmavlobaSi, arc erT samkurnalo jgufSi ar dafiqsirebula ZuZus kibos SemTxvevebi.

orma SemTxveva makontrolirebelma, epidemiologiurma kvlevam, romelTagan erTi Catarda aSS-Si (n=339 ZuZus kibos SemTxvevebi da n=6.780 sakontrolo) da meore - did britaneTSi (n=398 ZuZus kibos SemTxvevebi da n=3.930 sakontrolo), jandacvis monacemebze dayrdnobiT ar gamoavlina mamakacis ZuZus kibos ganviTarebis riskis zrda 5 ARI-ebis gamoyenebiT (*ixile gafrTxilebebi da usafrTxoebis zomebi*). pirveli kvlevis monacemebiT ar gamovlenila dadebiTi kavSiri mamakacis ZuZus kibosTvis (SefardebiTi riski gamoyenebis ≥ 1 wlisTvis ZuZus kibos diagnostirebamde gamoyenebis < 1 welTan SedarebiT: 0.70; 95% CI 0.34, 1.45). meore kvlevaSi, savaraudo gansxvavebulobis koeficienti ZuZus kibosTvis romelic dakavSirebulia 5 ARI-ebis gamoyenebasTan ara-momxmareblebTan SedarebiT iyo 1.08; 95% CI 0.62, 1.87).

avodartis xangrZliv gamoyenebas da mamakacebis ZuZus kibos Soris kavSiri ar aris cnobili.

tamsulozini

tamsulozini swrafad (erTi kviris Semdeg) zrdis maqsimaluri Sardis nakadis siCqares gluvi kunTovani daZabulobis SemcirebiT winamdebare jirkvalsa da ureTraSi, Sesabamisad xsnis obstruqcias. is aseve aumjobesebs gamaRizianebeli da obstruqciuli simptomebis kompleqss, romelSic Sardis buStis arastbiluroba da qveda saSarde traqtis gluvi kunTebis daZabuloba TamaSobs didi rols.

pre-klinikuri usafrTxoebis monacemebi

ara-klinikuri kvlevebi ar ganxorcielebula *duodartTan* mimarTebaSi. dutasteridi da tamsulozinis hidroqloridi individualurad farTod iqna Sefasebuli cxovelebze toqsikurobis testebSi da miRebuli monacemebi Seesabameboda 5 alfa-reduqtazas inhibitorebis da alfa-adrenerguli blokerebis cnobil farmakologiur moqmedebas. Semdegi debulebebi asaxavs informacias calkeul komponentebze arsebul informacias.

- **კვანცეროგენები, mutagenezi**

dutasteridma da tamsulozinis hidroqloridma ar gamoavlina genotoqsiurobis raime maCvenebeli in vitro da in vivo testebis farTo speqtrSi.

dutasteridi

virTagvebSi Catarebul kancerogenobis testSi dutasteridma maRali dozebSi gamoiwvia saTesle jirkvalSi keTilTvisebiani intersticiuli ujredebis simsvneebis zrda (158-er klinikuri eqspozicia). Tumca, A fiqroben, rom endokrinuli meqanizmi, romelic CarTulia intersticiuli ujredebis hiperplaziis da adenomebis produqciaSi virTagvebSi, ar aris Sesabamisi adamianebisTvis. Tagvebze Catarebul kancerogenobis kvlevaSiAar gamovlenila raime klinikurad mniSvnelovani efeqti simsvnis profilze.

tamsulozini

virTagvebsa da Tagvebze Catarebuli kancerogenobis kvlevis mixedviT, tamsulozinis hidroqloridma warmoSva mdedrebSi sarZeve jirkvlebis proliferaciuli cvlilebebis momatebuli SemTxvevebi. es monacemebi, romlebic SesaZloa gamowveulia hiperprolaqtinemiIT da vlindeba mxolod maRali dozis pirobebSi, ganixileba rogorc klinikurad ararelevanturi.

● **reproduqciuli toqsikologia**

dutasteridi

dutasteridma gamoiwvia fertilobis Seqcevadi daqveiTeBa mamal virTagvebSi, romelic Seesabameba damatebiT reproduqciul organoebze 5 alfa-reduqtazas inhibirebis farmakologiur aqtivobas. mas ar gaaCnia raime klinikuri mniSvneloba, ramdenadac ar hqonda raime zegavlana spermis warmoSobaze, koncentraciaze an mobilobaze.

aRiniSna gareTa genitaliebis feminizacia dedali virTagvebis da bocvrebis mamrobiTi sqesis nayofSi dutasteridis peroralurad miRebisas. Tumca, dutasteridis intravenurma Seyvanam orsul rezus maimunebSi embriofetaluri ganviTarebisas 2010 nanogrami/cxoveli/dReSi doziT ar gamouwvevia dedis an nayofis toqsuroba. es doza warmoadgens sul mcire mravlobiTi potenciuri dRiuri dozis 186-jerads (nanogrami/kg sawyisi) 50 kg qalSi, romelic miRebulia 5 ml spermis eqspoziciiT (Tu xdeba 100% absorbcia) dutasteridiT namkurnaleb mamakacebSi.

tamsulozini

tamsulozinis hidroqloridis maRalma dozebma gamoiwvia fertilobis Seqcevadi daqveiTeBa mamrobiT virTagvebSi, romelic SesaZloa ganpirobebulia spermis Semcvelobis cvlilebiT an eaukulaciis darRveviT. tamsulozinis zegavlana spermis raodenobaze an spermis funqciaze ar aris Sefasebuli.

tamsulozinis hidroqloridis Terapiul dozaze maRali doziT miRebam orsul virTagvebSi da bocvrebSi ar gamoiwvia nayofis dazianeba.

farmaceutuli Taviseburebebi

damxmare nivTierebebis CamonaTvali

kaprilis mJavas mono-di-gliceridebi, butilhidroqsituluoli, Jelatini, gliceroli, titanis dioqsidi, gamoxdili wyali, mikrokristaluri celuloza, metakrilis mJava - eTilakrilatis kopolimeri, talki, trieTil citrati, karagenani, kaliumis qloridi, hipromeloza, saSualo jaWvis trigliceridebi, lecitini, karnaubis cvili, simindis saxamebeli, rkinis yviTeli oqsidi, rkinis wiTeli oqsidi, FD&C yviTeli 6

SeuTavsebloba

ar aris mocemuli

Senaxvis vada

Senaxvis vada miTiTebulia SefuTvaze.

Senaxvis specialuri pirobebi

inaxeba 30°C-mde.

SefuTvis forma da SigTavsi

duodartis kafsulebi SefuTulia Semdegi saxis daxuruli sistemis konteinerSi:

gaumWvirvale, TeTri feris maRali simkvrivis polieTilenis (HDPE) boTlebi polipropilenis bavSvis rezistentuli TavsaxuriT induqciur-daluqvis lainerebiT.

gamoyenebis/moxmarebis instruqcia

dutasteridi Seiwoveba kanidan, amitom qalebi da bavSvebi unda moeridon gaJonvad kafsulebTan kontaqtis (gafrTxilebebi da sifrTxilis zomebi da orsuloba da laqtacia). Tu mainc moxda kontaqt gaJonvad kafsulebTan, aucilebelia kontaqtis midamos sapniT da wyliT saswrafod dabana.

yvela samkurnalwamlo forma ar aris xelmisawvdomi yvela qveyanaSi.

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