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WHAT THE PAPER SAYS · WHAT IT DOESN'T · WHY IT MATTERS

Dargaggoonni sadii T cells yaalii erga argatanii waggootaaf dhukkuba malee lubbuun turan. Phase 1 trial'n bu'aa kana maaltu akka fide agarsiisuu hin danda'u

ReMIND T cells laboratory keessatti guddisaman, patient tokkoon tokkoon isaa dhiiga mataa isaa irraa hojjetaman, daa'imman fi dargaggoota 33 high-risk brain tumors qaban keessatti infused godhe. Cells kun proteins sadii cancer cells keessatti argamuu danda'an irratti deebii kennuuf expand godhaman. Patients sadii infusion jalqabaa irraa intervals dhukkuba malee ji'a 31.8, 41.2 fi 51.6 ol qabaatan; keessaa tokko scan criteria jalatti complete response ture. Aggressive brainstem-tumor group keessatti scan tokko illee trial'n dursee murteesse response threshold ga'uuf shrinkage yookaan disappearance gahaa hin agarsiifne. Early safety-and-dose trial walfakkaataan du'a tokko seera isaa jalatti dose dabaluu irratti akka lakkaa'amu gahaa serious ta'e galmeesse. Comparison group malee, study'n T cells bu'aa sadii sana fidan jechuu hin danda'u.

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Author Correction

Nature Medicine 22 July 2026 irratti competing-interests disclosure wording ifa gochuuf Author Correction baase. Barreeffamni sirreeffame asitti fayyadame; clinical data fi conclusions hin jijjiiramne.

Author Correction →

Dargaggoonni sadii T seelota yaalii erga argatanii waggootaaf dhukkuba malee lubbuun turan. Sadarkaa 1 yaaliin bu'aa kana maaltu akka fide agarsiisuu hin danda'u

Ji'a 31.8 ol. Ji'a 41.2 ol. Ji'a 51.6 ol.

Kun interval dhukkuba hin galmoofne sadii, infuushinii jalqabaa yaalii T seelii yaala irraa eegalee galmaa'an dha. Inni jalqabaa nama waggaa 14 kan medulloblastoma isaa yeroo hedduu deebi'e ture; hordoffiin yeroo dhukkubsataa'n qorannoo keessaa ba'etti dhaabbate. Inni lammaffaa nama waggaa 8 astroblastoma baay'ee muraasa ta'e qabu ture, cutoff barruu yeroo ga'u ammas itti fufaa ture. Inni sadaffaa nama waggaa 14 glioblastoma isaa deebi'e qabu ture, innis ammas itti fufaa ture.

Lakkoofsi ji'aa tokko klinikaalaa fi nama irraa fagoo fakkaachuu danda'a. As keessatti garuu dhugaa namaa sana ifatti qabachuuf karaa amanamaa qofa dha. barruun waggoonni sun namoota sanaaf akkam akka turan nutti hin himu. Garuu dargaggoonni sadii sammuu tumors balaa guddaa qaban, seelota sana erga argatanii booda yeroo waggootaan safaramu keessatti dhukkuba galmaa'e malee lubbuun turan nuuf hima.

Seelota sun bu'aa kana fidan jechuu **hin agarsiisu**.

Garaagarummaan kun lafee dugdaa seenaa kanaa dha. ReMIND ifaa ture; jechuun maatii fi clinicians yaala kam akka kenname beeku turan. Akkasumas non-akka carraatti ramadame ture: walbira qabuu garee ramadame hin turre. Kana malees sadarkaa 1 ture, qorannoo jalqabaa multi-target T seelota oomishuun, kennuun fi dose obsamuu danda'uun qorachuun danda'amaa ta'uu jalqaba ilaaluuf ijaarame; survival fooyyessa moo miti jechuun qorachuuf miti. Seenaa klinikaa adda ta'e sadii galmeesse. Garuu aggressive brainstem-tumor garee keessatti scan tokko illee yaaliin dursee murteesse deebii daangaa ga'uuf shrinkage yookaan disappearance gahaa hin agarsiifne; serious events lama tumor swelling waliin walqabatan yaala waliin possibly related jedhame; akkasumas fatal event tokko seera yaalii jalatti dose dabaluu irratti akka ragaa mormii ta'u gahaa cimaa ture.

Waggoonni sun dhugaa dha. Sababni isaanii maal akka ta'e mirkanaa'aa miti. Dhugaan lamaan seenaa ijoo keessatti bakka qabu.

Yaala dhiiga dhukkubsataa tokkoon tokkoon isaa irraa hojjetame

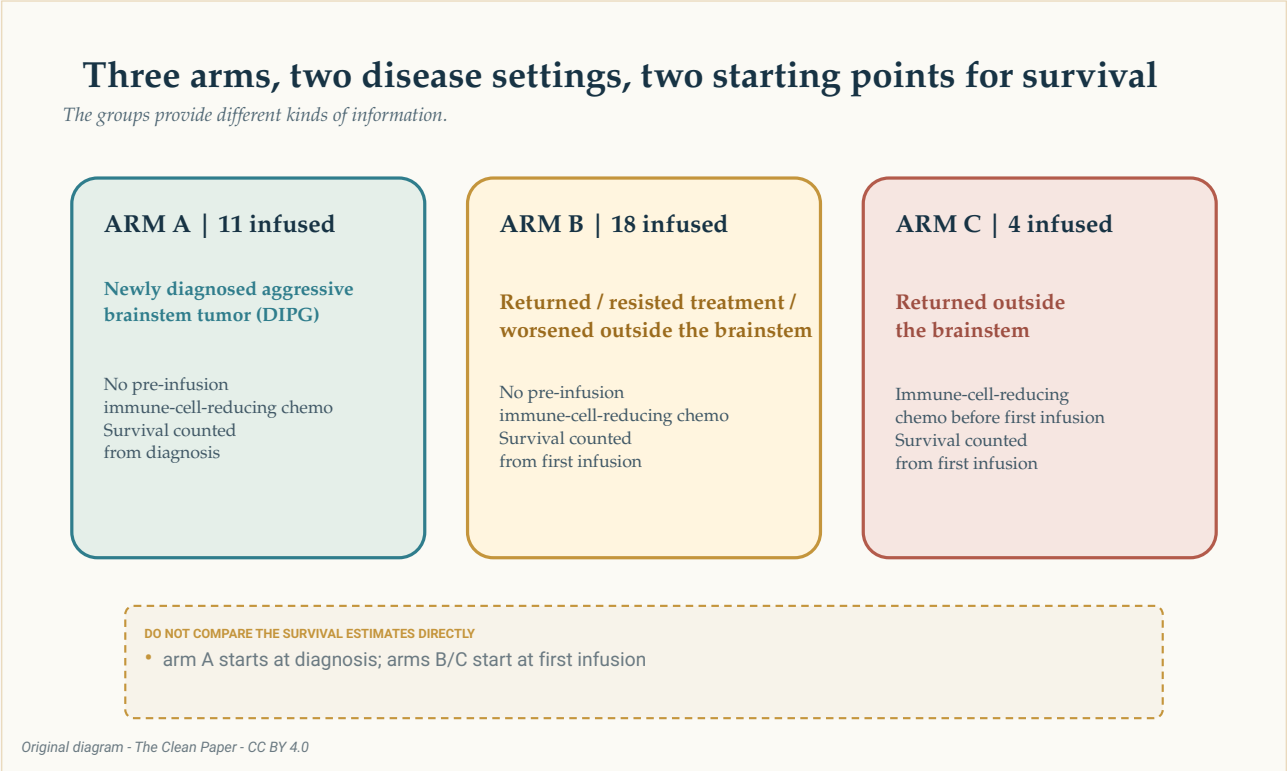
Yaala kun **TAA-T therapy** jedhama; gabaabinaan tumor-associated-antigen-specific T seelota. T seelota jechuun ittisa qaamaa seelota fragments molekiyuulii murtaa'an adda baasuu danda'an dha. Qorattoonni hirmaataa tokkoon tokkoon isaa irraa dhiiga walitti qaban; achii booda T seelota nama sanaa mataa isaa laaboraatoorii keessatti guddisan, yeroo wal fakkaatutti fragments pirootiinota tumor waliin walqabatan sadii itti agarsiisan: **WT1** (Wilms tumor 1), **PRAME** (preferentially expressed antigen in melanoma) fi **survivin**, pirootiinii seelii survival fi division keessatti hirmaatu. Pirootiinota kun pediatric sammuu tumors keessatti argamuu danda'u, ittisa qaamaa cellsf mallattoo ta'uu danda'u; garuu cancer qofaaf adda miti.

Isaan kun **CAR-T seelota** hin turre. CAR-T jechuun T seelota receptor laaboraatoorii keessatti qophaa'e, galma filatameef sensor haaraa ta'e, akka baatan genetic modification godhaman dha. ReMIND karaa adda ta'e fayyadame: T seelota uumamaan jiran, pirootiinii fragments sadii sanaaf deebii kennan filatee guddisuu; genetic engineering isaan irratti hin godhamne. Seelota qorataman, freeze godhaman, booda vein keessa kennaman. Galma tokko qofa mannaa sadii irratti xiyyeeffachuun, tumor seelii gosoota adda addaa irraa ijaarame keessatti seelota muraasni galma tokko qofa qabaachuu sababaan miliquu akka hin dandeenye carraa isaa xiqqeessuu qorattoonni abdatan.

> **Kun CAR-T irraa akkamitti adda?**
>
> CAR-T manufacturing T cellsf receptor nam-tolchee haaraa kenna, akka marker filatame kallattiidhaan adda baasan. TAA-T manufacturing receptor hin dabalu. Inni garee uummataa T seelota hin jijjiiramne walmakaa, receptors isaanii duraan jiran pirootiinii fragments WT1, PRAME yookaan survivin waliin walqabatan irratti deebii kennan, guddisa. Isaan kun karaalee immune-cell yaala hojjechuu adda addaa dha; ragaan mala tokko cancer tokko keessatti hojjeta jedhu mala biraatti dabarfamuu hin danda'u.

Kun tooftaa reasonable ta'e dha; kilinikaa adeemsa hojii mirkanaa'e miti. yaaliin seelota infused tumor murtaa'e keessa seenan, achitti turan yookaan isa ajjeesan hin agarsiifne. Gaaffiiwwan primary isaa bu'uuraa turan: product fayyadamuu danda'amu hojjechuun ni danda'amaa? kennuun ni danda'amaa? dose kam gara fuulduraatti geeffamuu qaba? toxicities maal mul'atan?

ReMIND Children's National Hospital keessatti gareewwan sadii galmeesse. **Arm A** keessatti **diffuse intrinsic pontine glioma (DIPG)** haaraa diagnose godhame, tumor aggressive pons keessa babal'atu, pons immoo kutaa brainstem keessaa tokko, surgery'n baasuun rakkisaa ta'e, ture. **Arm B** keessatti tumors sammuu fi spinal cord brainstem alaa deebi'an, yaala dandamatan yookaan hammaatan turan. Gareen lamaanuu lymphodepletion hin arganne; kun chemotherapy yeroo gabaabaa ittisa qaamaa seelota qaama keessatti duraan jiran keessaa muraasa yeroo muraasaaf gadi buusu, immune-cell infuushinii dura kennamu dha. **Arm C** immoo non-brainstem tumors deebi'an keessatti expansion dhukkubsattoota afur ture; pre-infusion chemotherapy kana fludarabine fi cyclophosphamide fayyadamuun dabale.



ReMIND arms sadii dhukkuboota adda addaa fi chemotherapy infuushinii dura fayyadamuu irratti garaagarummaa qaban fayyadame. Arm A keessatti survival adda-baafannaa dhibee irraa safarame; arms B fi C keessatti survival TAA-T infuushinii jalqabaa irraa safarame. Kanaaf tilmaamota isaanii kallattiidhaan walbira qabamuu hin danda'an.

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Namoonni shantamii tokko walii galan; soddomii sadii infuushinii argatan

Lakkoofsi dhukkubsattoota tarkaanfii hojii tokkoon tokkoon irratti ni xiqqaate.

Dhukkubsattoota shantamii tokko consent kennan. Namoota afurtamii saddeet irraa dhiigni walitti qabame. Isaan 48 keessaa afurtamii tokko, jechuun 85.4%, TAA-T product dose jalqabaa yaaliin karoorfate yookaan isaa ol irratti manufactured godhame argatan. Namoonni soddomii sadii yoo xiqqaate infuushinii tokko argatan: arm A keessatti 11, arm B keessatti 18, arm C keessatti 4.

Dhukkubsattoota tokko tokko yaala dura eligibility dhaban yookaan du'an. Dhukkubsattoota torba dhiigni isaanii walitti qabame dose sadarkaa jalqabaa yaalii irratti product fayyadamuu danda'amu hin arganne: jaha keessatti seelota laaboraatoorii keessatti gahaa hin baay'anne; tokko keessatti product qulqullina sakatta'a dirqama ta'e kufe. Dhukkubsattoota sagal yield jalqabaa gahaa hin turre dose gadi aanaatti irra deebi'anii ramadamuu qaban.

Adeemsi kun qorannoo keessatti fooyya'e. Dhiiga baay'inaan walitti qabuu fi akka seelota guddifaman jijjiiruu booda, dhukkubsattoota 14 jijjiirama sana booda dhiigni isaanii walitti qabame hundi yoo

xiqqaate yaala dose tokko, dose jalqabaa yaalii yookaan isaa ol, oomishuu danda'an. Kun yaala hojjechuun danda'amaa ta'uu irratti ragaa dhugaa dha. Bu'aa dhukkubsataa irratti ragaa miti.

yaaliin dhukkubsattoota 51 consent kennan irraa jalqabee 33 infuushinii kenne. Namoonni 18 hin geenye ragaa keessaa kutaa dha: dhiiga walitti qabuu, yaala hojjechuu, seera yaalii ammas guutuu fi fayyaan hammaachuu hundi eenyu yaala bira akka ga'e murteessan.

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istaatistikii dose-safety moodeela isaa fayyadamuun, qorannoon galma **tilmaamame body fuula bal'ina meetira iskuweerii tokkoon tokkoon isaaf dose tokko keessatti seelota miliyoona 80 (8 × 10^7 seelota/m^2)** filate. Body fuula bal'ina jechuun tilmaama klinikaa guddina qaama waliigalaa, dheerina fi ulfaatina irraa shallagamu dha; doctors bakka gogaa tokko, sammuu yookaan tumor safaran jechuu miti. Oncology fi pediatric yaaliiwwan dhukkubsattoota guddina adda addaa qaban keessatti dose karoorfame safartuu gochuuf fayyadamu. Fakkeenyaaf, dhukkubsataa body fuula bal'ina 1.2 m^2 jedhamee tilmaamame infuushinii tokkoof galma seelota miliyoona 96 qabaata. moodeelli dose seelota miliyoona 80/m^2 sana tilmaamame maximum tolerated dose, jechuun dose ol'aanaa yaaliin unacceptable-toxicity daangaa gadi turuu eegu, jedhe. Jechi kun barbaachisaa dha: dhukkubsattoota yaala argatan irratti mul'ate toxicity ceiling tokko hin geenye. Kun sadarkaa 2 qorannoof recommendation moodeela irratti hundaa'e ture; dose kun bal'inaan nageenya qabu ta'uu isaa ragaa miti.

Side dhiibbaawwan galmaa'an keessaa baay'een isaanii salphaa yookaan giddu-galeessaa turan. Fatal event tokko seera dose-limiting toxicity guute

taatee miidhaa jechuun rakkoo fayyaa kamiyyuu qorannoo keessatti galmaa'e; yaala irraa dhufe jechuu ofumaan miti. Grade 1 fi 2 jechuun salphaa yookaan giddu-galeessaa, grade 3 severe, grade 4 life-threatening, grade 5 death dha. ReMIND guutuu keessatti taateewwan miidhaa 332 galmaa'an keessaa 293, jechuun 88%, grade 1 yookaan 2 turan. Wanti yeroo baay'ee mul'ate mataa dhukkubbii, fatigue yookaan lethargy, nausea fi vomiting ture. Dhukkubsattoota 33 infused keessaa sadii grade 3 yookaan isaa ol events yaala booda jalqaban yookaan hammaatan, TAA-T therapy waliin yoo xiqqaate possibly related jedhamee ilaalame qabaatan. Dhukkubsattoota lama serious events edema, jechuun sammuu yookaan tumor keessa yookaan naannoo isaa swelling, waliin walqabatan, possibly related jedhame qabaatan.

Isaan keessaa tokko **P27**, dhukkubsataa DIPG qabu ture. Infuushinii booda guyyaa kudhanitti, P27 hydrocephalus, jechuun fluid sammuu keessa balaa geessisuu danda'uun walitti qabamu, tumor swelling fi breathing distress waliin qabaate. Doctors shunt jedhamu tube drainage kaa'anii fi steroid yaala swelling hir'isuuf dabalan booda dhukkubsataa'n hin fooyya'in. Fatal event sun **grade 5 dose-limiting toxicity** jedhamee classified godhame: protocol jalatti dose dabaluu itti fufu irratti akka lakkaa'amu gahaa serious ture.

Nageenya galmee yaalii mataa isaa attribution judgments lama yeroo tokko keessatti qaba: event sun TAA-T therapy waliin possibly related, underlying dhibee waliin immoo tarii related jedhamee ilaalame. Imaging'n tumor progression waliin walsime. Qorannoon sababaa tokko qofa filachuu hin danda'u; barreeffamni waa'ee isaa barreessus akkasuma filachuu hin qabu.

Duuti sun enrollment yeroo muraasaaf dhaabsiise. Protocol'n neurological stability yeroo dheeraa fi radiation fi infuushinii jalqabaa gidduu interval gabaabaa akka barbaachisu jijjiirame. Sana booda arm A keessatti dhukkubsattoota shan dose karoorfame walfakkaataa yookaan isaa ol argatan; event biraa seera dose-limiting guutu hin mul'anne.

Serious event lammaffaan **P42** keessatti mul'ate; inni diffuse midline glioma hammaachaa jiru thalamus, kutaa sammuu gadi fagoo, keessatti qaba ture. Infuushinii booda guyyaa kudha jahatti magnetic rezonaansii imaging (MRI) sammuu swelling mataa dhukkubbii fi neurologic symptoms biroo waliin agarsiise. Bevacizumab, qoricha tumor-associated swelling hir'isuu danda'u, erga kennamee booda symptoms sadarkaa isaanii duraa deebi'an. Event kun seera dose-limiting hin guunne.

Arm C keessatti dhukkubsattoota afran hundi temporary grade 3 cytopenias, jechuun blood-cell counts gadi aanaa, pre-infusion chemotherapy irraa eegamu qabaatan; events kun walitti makame TAA-T nageenya xiinxala keessaa baafaman. Hirmaataa tokko qorannoo guutuu keessatti yeroo booda ulaagaalee mild cytokine gadhiisuu syndrome, inflammatory reaction qaama guutuu keessatti ittisa qaamaa seelota activate yeroo ta'an uumamuu danda'u, guute.

Murtiin madaalawaan TAA-T yaala sadarkaa 1 cohort xiqqaa kana keessatti waliigalaan tolerable ture jechuu dha. Jecha daangaa hin qabne **nageenya qabu** jechuun guddina qorannoo, serious swelling

events lama fi fatal dose-limiting toxicity sana haqee dhiisa.

Cohorts keessatti maal ta'e

Kilinikaa gareewwan uummataa lamaan adda tursiifamuu qabu.

Arm A, garee DIPG, keessatti median progression-free survival, jechuun yeroo hanga tumor hammaatu yookaan dhukkubsataa du'utti, **adda-baafannaa dhibee irraa ji'a 10.5** ture. Median waliigalaan survival, jechuun yeroo dhukkubsattoota lubbuun turan, **adda-baafannaa dhibee irraa ji'a 13.7** ture. Dhukkubsattoota kudhan scans protocol'n dursee murteesse deebii rules fayyadamuun madaalamuu danda'an qabaatan: jaha tasgabbaa'aa dhibee, jechuun deebii jedhamee lakkaa'amuuf shrinkage gahaa hin qabne, progression jedhamee lakkaa'amuuf growth gahaa hin qabne; afur progressive dhibee qabaatan. **Scan tokko illee yaaliin dursee murteesse daangaa objective deebii ga'uuf shrinkage yookaan disappearance gahaa hin agarsiifne.**

Arms B fi C non-brainstem tumors adda addaa deebi'an, yaala dandamatan yookaan hammaatan walitti pool godhan; arm C qofti hiika qabu walbira qabuu'f baay'ee xiqqaa ture. As keessatti survival **infuushinii jalqabaa** irraa lakkaa'ame, adda-baafannaa dhibee irraa miti. Median yeroo tumor hammaachuu yookaan du'a dura **ji'a 5.0**, median yeroo lubbuun turan immoo **ji'a 12.7** ture; lamaan infuushinii irraa safaraman. Tilmaamota kun lakkoofsa arm A adda-baafannaa dhibee irraa eegalu waliin kallattiidhaan walbira qabamuu hin danda'an.

Arms B fi C keessatti dhukkubsattoota kudhan measurable dhibee, jechuun yoo xiqqaate tumor bal'ina tokko scan irratti amansiisaan safaramuu danda'u, qaban keessaa shan tasgabbaa'aa dhibee fi shan progressive dhibee qabaatan. Dhukkubsattoota tasgabbaa'aa dhibee jechuun classified godhaman shan keessaa tokko, P37, lesion hir'ina 90% ol qabaate, garuu scan lammaffaa mirkaneessu dura fayyaan isaa hammaate. Partial deebii jechuun shrinkage protocol'n dursee murteesse daangaa ce'u fi yeroo baay'ee scan booda mirkaneessu barbaada; kanaaf protocol'n bu'aa P37 partial deebii jedhee hin classify goone.

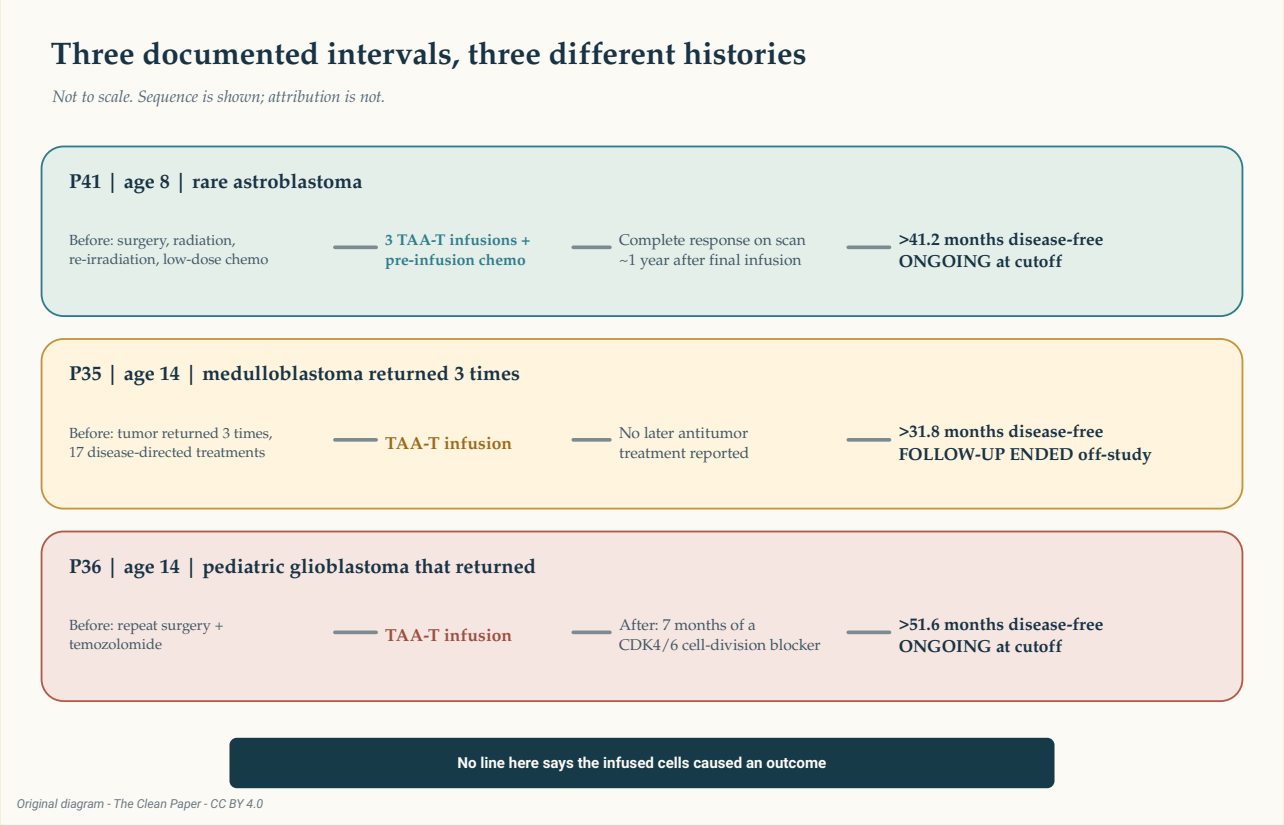
Dhukkubsattoota dabalataa shan dhibee nonmeasurable garuu evaluable ta'e qabaatan: doctors scan irratti jijjiirama madaaluu danda'an, garuu tumor bal'ina tokko illee reliable hammamtaa safartuu'f hin gahin. Isa gaarii deebiiwwan isaanii guutuu deebii tokko, tasgabbaa'aa dhibee sadii fi progressive dhibee tokko turan. Guutuu deebii sun P41 ture. Scan rules protocol jalatti, "guutuu deebii" jechuun mul'ataa non-target dhibee bade jechuu dha; cure mirkanaa'e jechuu miti. Measurable galma lesion tokko keessatti reliable dhibbeentaa hir'ina miti, kanaaf count dhukkubsattoota kudhan measurable dhibee sana keessa galuu hin qabu.

> **Radiologists deebii akkamitti classify godhu?**
>
> Yaala dura radiologists "galma" lesions, jechuun lesions guguddoo fi yeroo hedduu safaruuf ifa ta'an, adda baasu. Dhibee mul'atu kan biraa "non-target" dhibee jedhamee hordofamuu danda'a, garuu dhibbeentaa jijjiirama amansiisaa tokko itti hin kennamu. Partial deebii safarame galma lesions keessatti shrinkage gahaa fi yeroo baay'ee scan booda mirkaneessu

> barbaada. Guutuu deebii immoo scan ulaagaalee hojii irra jiru jalatti disappearance barbaada. Labels kun yeroo murtaa'e keessatti images ibsu; ofumaan cure hin mirkaneessan, yaala kam jijjiirama sana akka fide illee adda hin baasan.

Jireenya sadii, seenaa ragaa adda addaa sadii

Intervals dheeraan sadan yeroo hima tokko keessatti walitti cuunfaman salphaatti dogoggoraan hi-ikamu. Seenaa yaala isaanii fi safartuu daangaalee isaanii walfakkaataa hin turre.



P41, P35 fi P36 tokkoon tokkoon isaanii infuushinii jalqabaa booda interval dhukkuba galmaa'e malee dheeraa qabaatan; garuu treatments duraa, treatments booda, sadarkaa jalqabaa measurability fi hordoffii status isaanii adda addaa turan. Timelines tartiiba agarsiisu, causation miti.

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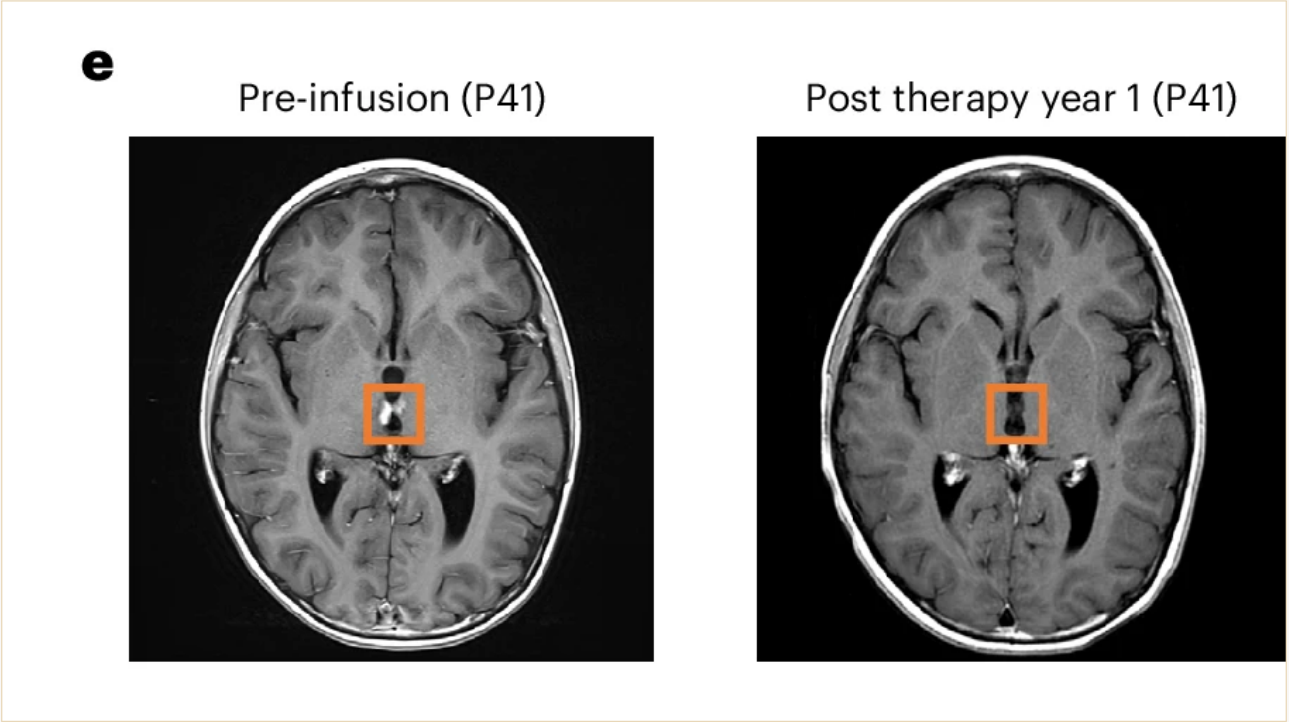
P41: guutuu deebii sadarkaa jalqabaa rakkisaa waliin

P41 waggaa 8tti yaalii seene; **astroblastoma deebi'ee fi EWSR1-BEND2 jiinii rearrangement qabu**, amaloota tumor baay'ee muraasa ta'e keessatti jiinota lama walitti makaman, qaba ture. Tumor sun sadaffaa ventricle, bakka fluid'n guutame sammuu keessa gadi fagoo jiru keessaa tokko, hirmaachise. Mucaan surgery'n tumor baasuu fi focused radiation argatee ture; sana booda TAA-T dura ji'a torbaatti

radiation course lammaffaa, infuushinii dura ji'a lamaatti immoo low-dose chemotherapy xumure. P41 arm C seene, pre-infusion immune-lowering chemotherapy argate, achii booda TAA-T infusions sadii argate.

Specialists sammuu scans irra deebi'anii dubbisanii booda, sadarkaa jalqabaa dhibee **nonmeasurable garuu evaluable** jedhamee classified godhame: mul'ataa fi jijjiirama isaa madaaluuf gahaa, garuu hammamtaa amansiisaan safaruuf mijataa miti. Dhumaa infuushinii booda waggaa tokkootti dhiyaatee, non-target lesion dhabamuun barreessitoonni complete-response classification imaging irratti godhan deeggare. Madda daataan interval dhukkuba hin galmoofne **infuushinii jalqabaa irraa ji'a 41.2 ol**, cutoff 1 January 2026tti ammas itti fufaa ture, agarsiisa.



Post-contrast T1-weighted MRI images kun P41 infuushinii dura fi dhumaa infuushinii booda waggaa tokko agarsiisu. Orange squares barreessitoonni qorannoon dabalaman, naannoo lesion enhancing infuushinii dura turee waggaa 1tti hin mul'anne mallatteessu; barreessitoonni kana guutuu deebii jedhanii classified godhan. Dhabamuun kun ilaalcha dhugaa fi abdachiisaa dha, garuu haala tokko kun maal akka isa fide nutti himuu hin danda'u: sadarkaa jalqabaa dhibee P41 evaluable ture garuu amansiisaan measurable hin turre, mucaan TAA-T dura re-irradiation fi chemotherapy argatee ture, deebii'n tursee mul'ate, yaaliin garee to'annoo hin qabu ture.

Gomez et al. / Nature Medicine CC BY-NC-ND 4.0

Kun ilaalcha yaalii keessaa isa nama hawwatu keessaa tokko, yeroo wal fakkaatutti sababa-qabeessa seenaa isaa keessaa isa laafaa dha. Natural seenaa tumor sanaa guutuutti hin beekamu. Hamma viable tumor sadarkaa jalqabaa irratti jiru confirm gochuun rakkisaa ture. Re-irradiation fi chemotherapy seelota dura dhufan. Deebii'n delayed ture, garee to'annoo immoo hin turre.

Ittisa qaamaa ragaan qaawwa sana hin cufu. Qorannoon **ELISpot assay**, laaboraatoorii qormaata yeroo T seelota galma filatameef deebii kennan mallattoolee isaan gadi lakkisan adda baasu, fayyadame. P41 manufactured seelota jalqabaa xiinxala rules qorannoo jalatti negaatiivii qoran. Pooziitivii bu'aa tokko less-strict reanalysis jalatti qofa mul'ate, booda false-positive concerns

sababaan keessaa baafame; qormaata plate'n cracked ture, leakage ta'uu danda'a ture, product reqoruuf hafe hin turre. Qorattoonni infused seelota unique T-cell-receptor fingerprints isaanii, **clonotypes** jedhaman, fayyadamuun hordofuus hin dandeenye. Product fingerprints kam infuushinii keessaa akka dhufe murteessuuf hafe hin turre; boodaa mixed immune-cell saamudawwan dhiiga irraa fudhataman immoo broad xiinxala qofaaf fayyadaman, kallattii product-to-blood match'f miti. Kanaaf saamudawwan jiran long-term persistence yookaan expansion seelota infuushinii product irraa dhufan kallattiidhaan mirkaneessuu hin dandeenye.

> **Qormaatawwan ittisa qaamaa kun maal agarsiisuu danda'u?**
>
> ELISpot T seelota laaboraatoorii keessatti galma filatameef saaxilame yeroo ta'an mallattoo gad lakkisu moo miti gaafata. Receptor-fingerprint tracking immoo T seelii families infuushinii product keessatti argaman sana booda dhiiga yookaan tishuu keessatti irra deebi'anii argamuu fi safaramuu danda'u moo miti gaafata. Bu'aan amansiisaan galma recognition irraa gara persistence'tti chain ragaa tokko deeggaruu danda'a; ta'us seelota kilinikaa deebii fidan jechuu hin mirkaneessu. As keessatti teknikaa rakkoowwan fi matched saamudawwan dhabamuun chain deeggarsa sana illee guutuu hin goone.

Kanaaf qorannoon P41 infused seelota galma yaadaman adda baasan, qaama keessa turan yookaan guutuu deebii fidan hin agarsiifne.

P35: ji'a 31.8 ol, achii booda hordoffii dhaabbate

P35 waggaa 14tti grade 4 medulloblastoma, high-grade sammuu cancer, qabaatee seene; jalqaba waggaa 7tti diagnose godhame ture. Enrollment yeroo ga'u dhibee yeroo sadii deebi'ee, dhukkubsataa'n **disease-directed treatments 17** argatee ture.

TAA-T booda, barruun additional antitumor yaala malee scans irratti stability dheeraa gabaasa. Madda daataan interval dhukkuba hin galmoofne **infuushinii jalqabaa irraa ji'a 31.8 ol** galmeessa. Yeroo sanatti P35 qorannoo keessaa ba'e. Qorannoo istaatistikii keessatti ilaalcha sun **censored** ture: wanta sana booda ta'e irratti yaada bu'uuraa tokko illee osoo hin godhin, hordoffii achitti dhaabbate. Interval sun hanga dhumaa cutoff barruu'tti dheerachuu hin qabu.

sadarkaa jalqabaa irratti dhibee amansiisaan safaramuu yookaan scan irratti deebii classify gochuuf gahaa madaalamuu hin dandeenye. Seenaa yaala baay'ee dheeraa fi akka carraatti ramadame comparator dhabamuun interval sana intervention tokko qofatti kennuun hin danda'amu.

P36: surgery fi chemotherapy dura, targeted yaala booda

P36 waggaa 14tti pediatric glioblastoma istaandaardii chemotherapy plus radiation fi investigational **PARP inhibitor**, qoricha tumor seelota DNA miidhame repair gochuuf karaa tokko block gochuuf yaadame, irratti progression booda deebi'e qabaatee seene. Tumor'n infuushinii jalqabaa dura ji'a sadii keessatti progress godhe; TAA-T dura repeat surgery fi temozolomide chemotherapy itti aane.

Socho'aa TAA-T yaala yeroo jiru disease-directed therapy hin kennamne; garuu dhumaa infuushinii booda P36 ji'a torbaaf **CDK4/6 inhibitor**, targeted drug seelii division suuta gochuuf qopheesse, argate. Madda daataan interval dhukkuba hin galmoofne **infuushinii jalqabaa irraa ji'a 51.6 ol**, qorannoo cutoff yeroo ga'u ammas itti fufaa ture, galmeessa.

Interval kun sadan keessaa isa dheeraa dha. Garuu tartiiba surgery, chemotherapy, TAA-T fi targeted yaala booda keessaa argama. yaaliin dhiibbaawwan isaanii adda baasuu hin danda'u.

Maaliif "booda" jechuun "sababaan" ta'uu hin danda'u

Vignettes kun daangaawwan isaanii waliin yeroo tursiifaman qofa hiika sirrii qabu.

ReMIND akka carraatti ramadame hin turre, concurrent garee to'annoo hin qabu ture, akkasumas yaala hojjeta moo miti qoruuf gahaa guddaa yookaan designed hin turre. Arms B fi C diagnoses adda addaa, hamma dhibee, duraa treatments fi dhibee courses eegaman walitti maku; isaan pool gochuun researchers daataa erga arganii booda descriptive choice godhan ture. Arm C pre-infusion immune-lowering chemotherapy dabale, arm B garuu hin daballe. Dhukkubsattoota tokko tokko TAA-T booda additional therapy argatan. Namoonni progression malee turan jalqaba irratti tumor baay'ee xiqqaa mul'atu qabu turan; kun mataan isaa bu'aa irratti dhiibbaa qabaachuu danda'a.

ClinicalTrials.gov fi barruun participation karaa adda addaatiin lakkaa'u. Registry yeroo ammaa namoota 33 hirmaatan jedhee tarreessa, ijoo nageenya safartuu isaa guyyaa 42 jalqabaa irratti xiyyeeffata. Barruu fi protocol namoota 51 consent kennan irraa jalqabu, namoota 33 infused ta'an gabaasu, gaaffiiwwan isaanii ijoo nageenya, yaala hojjechuu fi kennuun danda'amaa ta'uu, fi dose kam gara fuulduraatti geeffamuu qabu jedhu. Barreeffamni kun counting sirnoota lama walitti makuu mannaa definitions barruu fi protocol fayyadama.

Caveats kun keessaa tokko illee intervals sadii sana barbaachisummaa isaanii hin dhabsiisu. Isaan ragaan sun barbaachisummaa akkamii baachuu akka danda'u murteessu.

Bu'aan kun **preliminary mallattoo** dha: strategy kana qorannoo faayidaa tilmaamuuf qopheesse keessatti, biological safartuuwwan caalaa ifa ta'an fi walbira qabuu garee yaala selection, timing fi kunuunsa biroo irraa adda baasuu danda'u waliin qoruuf sababa dha. T seelota mucaa sadii cure godhan jechuun ragaa miti. Seelota sun blood-brain barrier, jechuun daangaa protective dhiiga circulation keessaa fi sammuu tishuu gidduu jiru, ce'anii tumors ajjeesan jechuun ragaa miti. Yaala maatiin yeroo ammaa research alatti gaafachuu danda'an miti.

Maaltu itti aanu

Gaaffiin hojiirra oolu ReMIND—yaala hojjechuu fi kennuun ni danda'amaa?—lakkoofsa lama barbaada. Dhukkubsattoota 48 dhiigni isaanii walitti qabame keessaa 41'f TAA-T product dose jalqabaa yaaliin karoorfate yookaan isaa ol irratti manufactured godhame; dhukkubsattoota 51 consent kennan keessaa 33 immoo yoo xiqqaate infuushinii tokko argatan. Adeemsi yaala hojjechuu illee yaalii

keessa fooyya'e. Seenaa klinikaa kun hojii itti aanu ni justify godha, garuu qorannoo itti aanu gaaffii adda ta'e gaafachuu qaba.

Qorattoonni seelota galma isaanii yaadaman amansiisaan adda baasu moo miti, eessa deemu, yeroo hammam turu fi bu'aawwan kunuunsa biroo waliin walbira qabamee fooyya'u moo miti mirkaneessuu qabu. Qorannoon guddaan uncommon harms ibsuuf illee barbaachisa. Fuuldura yaalii faayidaa qoruuf qopheesse garaagarummaa sadarkaa 1 qorannoo kun furuu hin dandeenye eeguu qaba: tumor gosa, hamma dhibee, pre-infusion chemotherapy, duraa yaala fi yaala booda kennamu.

Maatii pediatric sammuu tumors waliin falmaa jiraniif, shakkii jechuun duwwaa jechuu miti. Intervals dheeraa sadii waadaa godhamuu malee xiyyeeffannoo argachuu danda'u. Abdii kabajaa qabu keessaa isa guddaan, wanta amma illee hin beekamne hammam akka ta'e dhugaan himu dha.

Editorial note: lakkoofsi maal baachuu hin danda'u

Seenaa kun mucaan hundi cure ta'ee xumurama jennee hawwuun uumamaa dha. Akkas hin xumuramu. ReMIND dhukkuboota maatiin filannoo baay'ee rakkisaa qunnamuu danda'an, clinicians immoo yaalii yaala gargaaru, homaa hin jijjiiru yookaan miidhaa fida moo miti osoo hin beekin murteessuu qaban keessatti gaggeeffame.
Qorannoon intervals dhukkuba malee dheeraa galmeesse. Serious taateewwan miidhaa fi du'a P27 illee galmeesse. Investigators fatal event sana TAA-T waliin possibly related, underlying dhibee waliin tarii related jedhanii madaalan; imaging'n progression waliin walsime. Shakkii sun booda irraa furamuu hin danda'u, blame taasisuunis hin qabu.
Koodii P27 iccitii dhuunfaa mucaa tokkoo eega. Garuu mucaa sana abstract gochuu hin qabu. Dhukkubsataa lakkoofsa tokkoon tokkoon duuba dargaggeessa tokko, maatii dhiibbaa keessatti murtii fudhatu, fi kilinikaa team haala option tokko illee certainty hin qabne keessatti kunuunsa irratti itti gaafatamummaa qabu ture. Hirmaachuun isaanii bu'aa abdachiisaa yookaan "heroic" uumuuf dirqama isaan irratti hin kaa'u; research booda irraa waan irraa baratuuf qofa duuti "gatii fudhatama qabu" hin ta'u.
Yaalaa progress treatments cure godhan qofaan hin uumamu. Sadarkaa 1 qorannoo maal manufactured fi delivered godhamuu akka danda'u mirkaneessuu, dose qorannoo itti aanuuf adda baasuu, harms kam xiyyeeffannoo barbaadu agarsiisuu fi protocol akkamitti jijjiiramuu akka qabu ibsuu danda'a. Beekumsi sun suffering haqee hin deebisu. Inni garuu amanamummaadhaan gabaasuu, qorannoowwan booda akka nageenya qabu caalaa ta'an itti fayyadamuu fi namoota isa akka danda'amu godhan yaadachuuf dirqama uuma.

Cuunfaa gabaabaa

ReMIND sadarkaa 1 yaalii jalqabaa T seelota hirmaataa tokkoon tokkoon isaa dhiiga mataa isaa irraa guddisamanii, laaboraatoorii keessatti pirootiinota sadii cancer seelota keessatti argamuu danda'an irratti deebii kennuuf expand godhaman ture. Daa'imman fi dargaggoota 51 balaa guddaa qabu sammuu yookaan spinal-cord tumors qaban consent kennan keessaa, 48 dhiigni isaanii walitti

qabame, 41 product dose jalqabaa karoorfame yookaan isaa ol irratti manufactured godhame qabaatan, 33 immoo yoo xiqqaate infuushinii tokko argatan. Rakkoowwan fayyaa galmaa'an keessaa baay'een salphaa yookaan giddu-galeessaa turan; garuu dhukkubsattoota infused sadii severe yookaan isaa ol events yoo xiqqaate yaala waliin possibly related jedhame qabaatan. Isaan keessaa lama serious sammuu- yookaan tumor-swelling events possibly related qabaatan; tokko du'a seera yaalii dose-limiting guute ture. Aggressive brainstem-tumor garee keessatti scan tokko illee shrinkage yookaan disappearance yaaliin dursee murteesse deebii daangaa ga'u hin agarsiifne. Non-brainstem gareewwan keessatti dhukkubsattoota dargaggoonni sadii infuushinii jalqabaa irraa intervals dhukkuba malee ji'a 31.8, 41.2 fi 51.6 ol qabaatan; keessaa tokko scan ulaagaalee jalatti guutuu deebii ture. Dhukkubsataa tokko qorannoo keessaa yeroo ba'u hordoffii dhaabbate; intervals lama biroo cutoff yeroo ga'u ammas itti fufaa turan. yaaliin garee to'annoo hin qabu ture, faayidaa mirkaneessuuf designed hin turre, yaalii T-cell therapy bu'aa sana fide jechuu hin danda'u.

Sakatta'a ifaa

Wanti barruu agarsiisu: Personalized T seelii product pirootiinota tumor-associated sadii irratti xiyyeeffate, dhukkubsattoota 48 dhiigni isaanii walitti qabame keessaa 41'f dose jalqabaa yaalii yookaan isaa ol irratti hojjetame; dhukkubsattoota 51 consent kennan keessaa 33 yoo xiqqaate infuushinii tokko argatan. istaatistikii moodeelli dose qorannoo itti aanuuf filate. yaaliin rakkoowwan fayyaa mul'atan galmeesse, akkasumas infuushinii booda intervals dhukkuba malee dheeraa sadii galmeesse.

Wanti abdachiisaa garuu hin mirkanoofne: Yaalii T seelota dhukkubsattoota tokko tokko keessatti dhibee to'annoo gumaachan ta'uu, keessumaa namoota jalqaba irratti tumor baay'ee xiqqaa mul'atu qaban keessatti, fi to'atame qorannoo booda clinically faayidaa qabu ta'uu danda'uu.

Wanti inni hin agarsiifne: Yaala'n daa'imman sadii cure godhe; guutuu deebii yookaan intervals dheeratan isa irraa dhufan; P41 infused seelota galma yaadaman adda baasuu yookaan qaama keessa turuu isaanii agarsiifame; mala kun aggressive brainstem tumor kana keessatti hojjeta; yookaan yaala kun yeroo ammaa jiru fi bal'inaan nageenya qabu dha jechuu.

Daangaawwan ijoo: Kun jalqabaa safety-and-dose qorannoo ture, keessatti namni hundi yaala maal akka ta'e beeka, namni tokko illee walbira qabuu grouptti tasaa hin ramadamne; dhukkubsattoota 33 diagnoses adda addaa qaban infuushinii argatan; mallattoon faayidaa jalqabaa gaaffii ijoo hin turre; survival gareewwan keessatti starting qabxiilee adda addaa irraa safarame; arm C dhukkubsattoota infused afur qofa qabaatee pre-infusion immune-lowering chemotherapy fayyadame; dhukkubsattoota tokko tokko therapies biroo argatan; haalawwan adda ta'an sadii jalqaba irratti tumor bal'ina scan irratti amansiisaan safaramuu danda'u hin qabne—P41 dhibee mul'atu doctors hordofuu danda'an qaba ture, P35 fi P36 garuu deebii classify gochuuf gahaa madaalamuu hin dandeenye; laaboraatoorii ragaa infused seelota bu'aawwan booda waliin kallattiidhaan walqabsiisuu hin dandeenye; akkasumas fatal event tokko seera toxicity yaalii keessaa isa hamaa guute.

Dubbisaan waliigalaa hammam amantaa qabaachuu qaba? Amantaa guddaa argannoowwan daangaa qabu yaala hojjechuu fi kennuu, fi rakkoowwan fayyaa garee kana keessatti galmaa'an irratti.

Amantaa guddaa intervals sadii galmaa'an infuushinii booda dhugumaan uumaman irratti. Amantaa gadi-aanaa yaalii T-cell therapy bu'aa sana fide jedhu irratti, sababni isaas yaalii kun gaaffii sana deebisuuf designed hin turre.

Maddoota

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