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

Matasa uku sun kasance da rai ba tare da cuta ba shekaru bayan karɓar T cells na gwaji. Gwajin phase 1 ba zai iya nuna abin da ya jawo waɗannan sakamakon ba

ReMIND ya yi infusion na T cells da aka girma a laboratory daga jinin kowane mara lafiya ga yara da matasa 33 masu high-risk brain tumors. An faɗaɗa sel ɗin domin su amsa ga furotin uku da za su iya kasancewa a cancer cells. Marasa lafiya uku sun sami disease-free intervals fiye da watanni 31.8, 41.2 da 51.6 daga infusion na farko, ciki har da complete response guda ɗaya bisa scan criteria. A aggressive brainstem-tumor group, babu scan da ya nuna isasshen raguwa ko bacewa da ta kai predefined response threshold na trial. Wannan early safety-and-dose trial ɗin ya kuma rubuta mutuwa guda da ta yi tsanani har ta kidaya a kan kara dose bisa ka'idodinsa. Ba tare da comparison group ba, binciken ba zai iya nuna ko T cells ne suka jawo outcomes ukun ba.

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Author Correction

Nature Medicine ta fitar da Author Correction a 22 Yuli 2026 domin fayyace wording a competing-interests disclosure. An yi amfani da corrected article a nan; clinical data da conclusions ba su sauya ba.

Author Correction →

Matasa uku sun kasance da rai ba tare da cuta ba shekaru bayan karɓar T cells na gwaji. Gwajin phase 1 ba zai iya nuna abin da ya jawo waɗannan sakamakon ba

Fiye da watanni 31.8. Fiye da watanni 41.2. Fiye da watanni 51.6.

Waɗannan su ne lokuta uku da aka rubuta na kasancewa ba tare da cuta ba tun daga infusion na farko na wani gwajin maganin T cell. Na farko ya kasance na wani ɗan shekara 14 wanda medulloblastoma ɗinsa ya dawo sau da yawa; lura ya ƙare lokacin da mara lafiyar ya bar binciken. Na biyu ya kasance na wani ɗan shekara 8 mai astroblastoma mai wuya, kuma lokacin yana ci gaba har zuwa ranar da takardar ta rufe bayanai. Na uku ya kasance na wani ɗan shekara 14 wanda glioblastoma ɗinsa ya dawo, kuma wannan ma yana ci gaba.

Kidayar watanni na iya yin kama da lambar asibiti mai nisa da rayuwar mutum. A nan ita ce hanya mafi gaskiya ta riƙe ainihin abin da ya shafi mutum a fili. takardar ba ta gaya mana yadda waɗannan shekarun suka kasance ga yaran da iyalansu ba. Amma ya gaya mana cewa matasa uku masu ciwace-ciwacen kwakwalwa masu babban haɗari sun kasance da rai ba tare da cuta da aka rubuta ba na tsawon lokacin da ake auna da shekaru bayan sun karɓi sel ɗin.

Ba ya gaya mana cewa sel ɗin ne **suka jawo** waɗannan sakamakon.

Wannan bambanci shi ne ginshiƙin wannan labari. ReMIND ya kasance open-label, wato iyalai da likitoci sun san wane magani aka bayar. Haka kuma ba randomized ba ne: babu wata ƙungiyar kwatanci da aka ware ta hanyar bazuwar. Kuma phase 1 ne, wato gwaji na farko da aka gina da farko domin auna ko za a iya ƙera T cells masu nufin targets da yawa, a ba su, kuma a nazarce su a dose da za a iya jurewa—ba domin a gwada ko suna ƙara tsawon rayuwa ba. Ya rubuta tarihin asibiti guda uku masu ban mamaki. Haka kuma ya rubuta cewa a ƙungiyar ciwon brainstem mai tsanani babu scan da ya nuna raguwa ko bacewa da ta kai predefined response threshold na gwaji ɗin; akwai serious events biyu da suka shafi kumburin tumor waɗanda wataƙila suna da alaƙa da maganin; kuma akwai mutuwa guda ɗaya da ta yi tsanani har ta ƙidaya a matsayin dalilin rashin ƙara dose bisa ƙa'idodin gwaji ɗin.

Shekarun gaskiya ne. Danganta su ga maganin ba ta da tabbas. Dukkan gaskiyoyin biyu sun cancanci zama a tsakiyar labarin.

Magani da aka yi daga jinin kowane mara lafiya

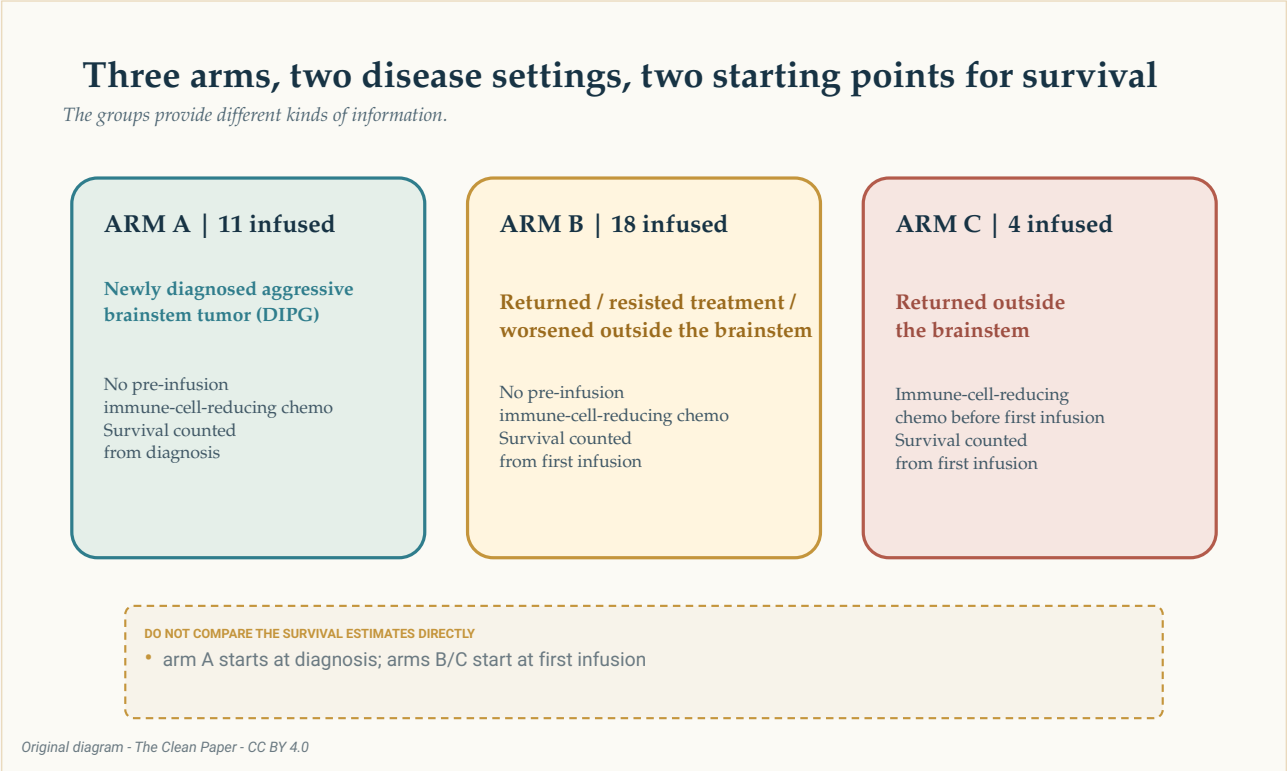
Ana kiran maganin **TAA-T therapy**, gajeren suna na tumor-associated-antigen-specific T cells. T cells sel ne na garkuwar jiki waɗanda za su iya gane wasu takamaiman gutsattsarin molecules. Masu binciken sun tattara jini daga kowane mahalarta, sannan suka girma T cells na mutumin a dakin gwaje-gwaje yayin da suke nuna musu gutsattsarin furotin uku da ke da alaƙa da tumors: **WT1** (Wilms tumor 1), **PRAME** (preferentially expressed antigen in melanoma) da **survivin**, wani furotin da ke da hannu a rayuwa da rabuwar sel. Waɗannan furotin na iya kasancewa a ciwace-ciwacen kwakwalwar yara kuma su zama kamar alamun da sel na garkuwar jiki za su gane, amma ba na cancer kaɗai ba ne.

Waɗannan ba **CAR-T cells** ba ne. CAR-T T cells ne da aka canja kwayoyin halittarsu domin su ɗauki receptor da aka ƙera a dakin gwaje-gwaje—wata sabuwar na'urar gano target da aka zaɓa. ReMIND ya yi amfani da wata dabara dabam: ya zaɓi kuma ya faɗaɗa T cells da suke faruwa a halitta waɗanda suka amsa ga gutsattsarin furotin ukun, ba tare da genetic engineering ba. An gwada sel ɗin, an daskare su, sannan daga baya aka saka su cikin jijiya. Ta hanyar nufin targets uku maimakon guda ɗaya, masu binciken sun yi fatan rage yiwuwar tumor da ya ƙunshi nau'ikan sel daban-daban ya tsere saboda wasu sel kaɗai ne ke ɗauke da target guda.

> **Ta yaya wannan ya bambanta da CAR-T?**
>
> A ƙera CAR-T, ana bai wa T cells wani sabon artificial receptor domin su gane alamar da aka zaɓa kai tsaye. A ƙera TAA-T ba a ƙara receptor. Ana girma cakuda T cells da ba a canja su ba, waɗanda receptors ɗinsu na asali suke amsa ga gutsattsarin furotin da ke da alaƙa da WT1, PRAME ko survivin. Waɗannan hanyoyi ne daban-daban na ƙirƙirar maganin immune-cell; shaida cewa dabara ɗaya tana aiki a wani cancer ba za a ɗauka kai tsaye zuwa ɗayar ba.

Wannan dabara ce mai ma'ana ta kimiyya, ba wani clinical mechanism da aka tabbatar ba. gwaji ɗin bai nuna cewa sel ɗin da aka yi infusion sun shiga wani tumor takamaimai, sun ci gaba da zama a can ko sun kashe shi ba. Tambayoyinsa na farko sun fi sauƙi: za a iya ƙera usable product? Za a iya bayar da shi? Wane dose ya kamata ya shiga gwaji na gaba? Waɗanne toxicities suka bayyana?

ReMIND ya shigar da ƙungiyoyi uku a Children's National Hospital. **Arm A** ya haɗa da sabbin masu ganewar **diffuse intrinsic pontine glioma (DIPG)**, wani tumor mai tsanani da ke yaɗuwa a cikin pons, wani ɓangare na brainstem, kuma yana da wuya a cire shi da tiyata. **Arm B** ya haɗa da tumors na kwakwalwa da spinal cord da ba na brainstem ba waɗanda suka dawo, suka ƙi magani ko suka tsananta. Babu ɗayan ƙungiyoyin biyu da ya samu lymphodepletion, wato ɗan gajeren chemotherapy da ke rage wasu sel na garkuwar jiki kafin immune-cell infusion. **Arm C** ƙarin ƙungiya ce ta marasa lafiya huɗu masu tumors da ba na brainstem ba da suka dawo, kuma ta ƙara wannan chemotherapy kafin infusion ta amfani da fludarabine da cyclophosphamide.



ReMIND ya yi amfani da arms uku masu cututtuka daban da kuma bambancin amfani da chemotherapy kafin infusion. An auna survival na arm A daga lokacin diagnosis; na arms B da C kuma daga TAA-T infusion na farko, saboda haka ba za a iya kwatanta estimates ɗin kai tsaye ba.

Mutane 51 sun ba da consent; 33 aka yi wa infusion

Adadin marasa lafiya ya ragu a kowane mataki na aikace-aikacen gwajin.

Marasa lafiya 51 sun ba da consent. An tattara jini daga 48. A cikin waɗannan 48, mutane 41, ko 85.4%, sun sami TAA-T product da aka ƙera a dose na farko da gwaji ya shirya ko sama da shi. Mutane 33 sun karɓi aƙalla infusion guda ɗaya: 11 a arm A, 18 a arm B da 4 a arm C.

Wasu marasa lafiya sun daina cika sharudda ko suka mutu kafin magani. Marasa lafiya bakwai da aka riga aka tattara jininsu ba su kai ga usable product a dose na farko da aka shirya ba: shida saboda sel ɗin ba su ninka sosai a dakin gwaje-gwaje ba, ɗaya kuma saboda product ɗin bai wuce quality check da ake buƙata ba. Marasa lafiya tara da farkon yield ɗinsu bai isa ba sai aka saukar da su zuwa ƙananan dose.

Tsarin ya inganta yayin binciken. Bayan an fara tattara jini mai yawa da sauya yadda ake girma sel ɗin, duk marasa lafiya 14 da aka tattara jininsu bayan waɗannan sauye-sauye sun samar da aƙalla dose guda ɗaya a dose na farko da gwaji ya shirya ko sama da shi. Wannan shaida ce ta gaske game da ikon ƙera maganin. Ba sakamakon lafiya na mara lafiya ba ne.

gwaji ɗin ya fara da marasa lafiya 51 da suka ba da consent kuma ya yi infusion ga 33. Mutane 18 da ba su kai infusion ba su ma wani ɓangare ne na shaidar: tattara jini, ƙera magani, ci gaba da cika ka'idodin gwaji da kuma tabarbarewar lafiya duk sun shafi wanda ya kai matakin magani.

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Ta amfani da statistical dose-safety model, binciken ya zaɓi target na **sel miliyan 80 a kowane dose ga kowace murabba'in mita na estimated body surface area (8 × 10^7 cells/m^2)**. Body surface area ƙididdigar asibiti ce ta girman jiki gaba ɗaya daga tsawo da nauyi; ba yana nufin likitoci sun auna wani ɓangaren fata, kwakwalwa ko tumor ba. Gwaje-gwajen oncology da na yara suna amfani da shi domin daidaita planned dose tsakanin marasa lafiya masu girman jiki daban—misali, mara lafiya mai estimated body surface area na 1.2 m^2 zai sami target dose na sel miliyan 96 a infusion guda. samfurin kuma ya kira dose na sel miliyan 80/m^2 estimated maximum tolerated dose—dose mafi girma da ake sa ran zai kasance ƙasa da unacceptable-toxicity threshold na gwaji. Kalmar "estimated" tana da muhimmanci: marasa lafiyar da aka yi wa magani ba su kai ga wani observed toxicity ceiling ba. Wannan recommendation ce daga model domin phase 2, ba hujja cewa dose ɗin yana da aminci gaba ɗaya ba.

Yawancin side effects da aka rubuta sun kasance mild ko moderate. Mutuwa guda ta cika ƙa'idar dose-limiting toxicity

Adverse event shi ne duk wata matsalar lafiya da aka rubuta yayin binciken; ba yana nufin maganin ne ya jawo ta kai tsaye ba. Grades 1 da 2 suna nufin mild ko moderate, grade 3 severe, grade 4 life-threatening, grade 5 kuma mutuwa. A duk ReMIND, 293 daga cikin adverse events 332 da aka rubuta, ko 88%, sun kasance grade 1 ko 2.

Abubuwan da aka fi gani sun haɗa da ciwon kai, gajiya ko kasala, tashin zuciya da amai. Marasa lafiya uku daga cikin 33 da aka yi wa infusion sun sami events na grade 3 ko sama waɗanda suka bayyana ko suka tsananta bayan magani kuma aka ɗauke su aƙalla possibly related da TAA-T therapy. Marasa lafiya biyu sun sami serious events da wataƙila suna da alaƙa da maganin, waɗanda suka haɗa da edema—kumburi a cikin ko kewaye da kwakwalwa ko tumor.

Ɗaya daga cikinsu shi ne **P27**, mara lafiya mai DIPG. Kwana goma bayan infusion, P27 ya samu hydrocephalus, wato taruwar ruwa mai haɗari a cikin kwakwalwa, tare da kumburin tumor da wahalar numfashi. Mara lafiyar bai inganta ba bayan likitoci sun saka bututun drain da ake kira shunt kuma suka ƙara steroid domin rage kumburi. An classified mutuwar a matsayin **grade 5 dose-limiting toxicity**: bisa protocol, ta yi tsanani isa ta ƙidaya a kan ci gaba da ƙara dose.

Safety record na gwaji ɗin yana riƙe da attribution judgments guda biyu a lokaci ɗaya: an ɗauki event ɗin a matsayin **possibly related to TAA-T therapy** kuma **probably related to the underlying disease**. Imaging ya dace da ci gaban tumor. Binciken ba zai iya zaɓar dalili guda ɗaya ba, kuma labarin da ke bayani game da shi bai kamata ya yi haka ba.

Mutuwar ta sa aka dakatar da enrollment na ɗan lokaci. An sauya protocol domin a buƙaci tsawon lokaci na neurological stability da kuma gajeriyar tazara tsakanin radiation da infusion na farko. Daga baya aka yi wa wasu marasa lafiya biyar na arm A magani a planned doses iri ɗaya ko sama, ba tare da wani event da ya sake cika dose-limiting rule ba.

Serious event na biyu ya faru a **P42**, wanda ke da diffuse midline glioma da ke tsananta a thalamus, wani ɓangare mai zurfi na kwakwalwa. Kwana 16 bayan infusion, magnetic resonance imaging (MRI) ya nuna kumburin kwakwalwa tare da ciwon kai da wasu neurological symptoms. Symptoms ɗin sun koma matakin da suke a baya bayan bevacizumab, magani da zai iya rage kumburin da tumor ke haddasawa. Wannan event bai cika dose-limiting rule ba.

Dukkan marasa lafiya huɗu a arm C sun sami temporary grade 3 cytopenias—ƙananan adadin blood cells—wanda ake sa ran zai biyo bayan chemotherapy kafin infusion; an cire waɗannan events daga combined TAA-T safety nazari. Mahalarta guda ɗaya a dukan binciken ya cika, a retrospective review, sharuddan mild cytokine release syndrome, wato inflammatory reaction na jiki gaba ɗaya da zai iya faruwa lokacin da immune cells suka kunna.

Ƙayyadadden conclusion shi ne cewa TAA-T magani ya kasance **generally tolerable** a wannan ƙaramin phase 1 cohort. Kalmar **safe** ba tare da ƙayyadewa ba za ta ɓoye ƙarancin girman binciken, serious swelling events biyu da fatal dose-limiting toxicity.

Abin da ya faru a cikin cohorts

Ya zama dole a riƙe clinical populations biyu a rarrabe.

A arm A, wato ƙungiyar DIPG, median progression-free survival—lokacin daga diagnosis har tumor ya tsananta ko mara lafiya ya mutu—ya kasance **watanni 10.5 daga diagnosis**. Median overall survival—lokacin da marasa lafiya suka kasance da rai—ya kasance **watanni 13.7 daga diagnosis**. Marasa lafiya goma suna da scans da za a iya tantancewa da predefined response rules na protocol: shida sun sami stable disease, wato babu isasshen raguwa da zai ƙidaya a matsayin response kuma babu isasshen girma da zai ƙidaya a matsayin progression; huɗu kuma

sun sami progressive disease. **Babu scan da ya nuna isasshen raguwa ko bacewa da za ta kai predefined threshold na gwaji domin objective response.**

Arms B da C sun haɗa tumors da dama da ba na brainstem ba waɗanda suka dawo, suka ƙi magani ko suka tsananta, domin arm C ya yi ƙanƙanta da za a iya yin kwatanci mai ma'ana da shi shi kaɗai. A nan an fara ƙidayar survival daga **infusion na farko**, ba daga diagnosis ba. Median time kafin tumor ya tsananta ko mara lafiya ya mutu ya kasance **watanni 5.0**, median time alive kuma **watanni 12.7**, duka daga infusion. Ba za a iya kwatanta waɗannan estimates kai tsaye da lambobin arm A da aka ƙidaya daga diagnosis ba.

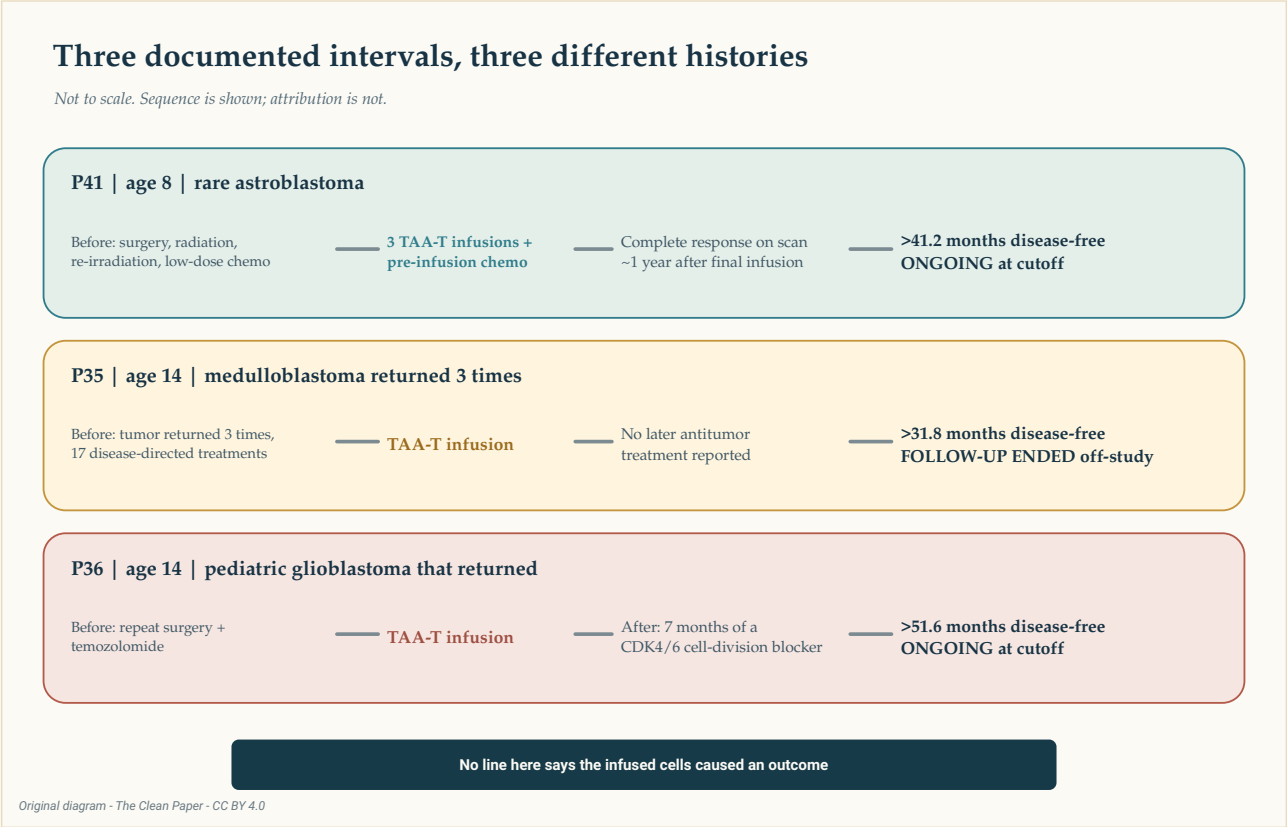
A cikin marasa lafiya goma na arms B da C masu measurable disease—wato aƙalla wani tumor area da za a iya auna girmansa cikin aminci a scans—biyar sun sami stable disease, biyar kuma progressive disease. Ɗaya daga cikin biyar da aka classified stable disease, P37, ya sami raguwar lesion fiye da 90% amma lafiyarsa ta tabarbare kafin scan na biyu ya iya tabbatar da sakamakon. Partial response yana buƙatar raguwa da ta ketare predefined threshold na protocol da kuma scan daga baya da zai tabbatar da ita, saboda haka protocol bai classified sakamakon P37 a matsayin partial response ba.

Wasu marasa lafiya biyar suna da cutar da ba za a iya auna ta ba amma har yanzu evaluable ce: likitoci za su iya tantance sauyi a scans, amma babu wani tumor area da ya cika sharuddan dependable size ma'auni. Best responses ɗinsu sun kasance complete response guda ɗaya, stable disease uku da progressive disease guda ɗaya. Complete response ɗin na P41 ne. Bisa scan rules na protocol, "complete response" yana nufin visible non-target disease ya bace; ba yana nufin an tabbatar da cure ba. Ba reliable percentage reduction ba ne a measurable target lesion kuma bai shiga cikin ƙidayar marasa lafiya goma masu measurable disease ba.

> **Ta yaya radiologists ke classified response?**
>
> Kafin magani, radiologists suna gano "target" lesions da suke da girma da bayyana sosai har za a iya auna su sau da yawa. Sauran visible disease za a iya bibiyarsu a matsayin "non-target" disease ba tare da ba su dependable percentage change ba. Partial response yana buƙatar isasshen raguwa a measured target lesions kuma yawanci scan daga baya domin tabbatarwa. Complete response yana buƙatar bacewa bisa scan criteria da ake amfani da su. Waɗannan labels suna bayanin hotunan wani lokaci takamaimai; ba sa tabbatar da cure da kansu kuma ba sa nuna wane magani ne ya jawo canjin.

Rayuka uku, labaran shaida uku daban

Lokuta ukun masu tsawo sun fi sauƙin a fahimce su ba daidai ba idan aka matse su cikin jumla guda. Tarihin maganinsu da iyakokin ma'auninsu ba iri ɗaya ba ne.

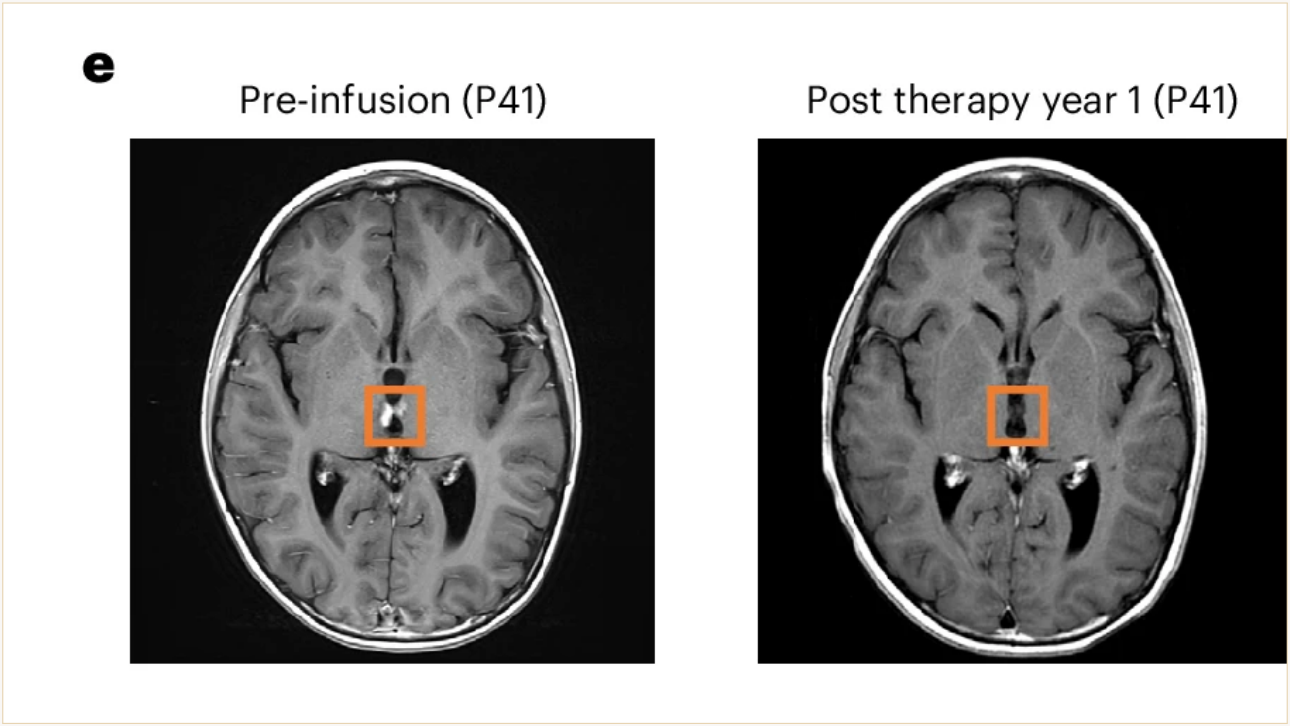


P41, P35 da P36 kowannensu yana da dogon disease-free interval da aka rubuta bayan infusion na farko, amma magunguna da suka samu kafin TAA-T, magunguna na baya, ko cutar za a iya auna ta a baseline, da matsayin follow-up sun bambanta. Timelines ɗin suna nuna jerin abubuwa, ba causation ba.

P41: complete response tare da baseline mai wahalar fassara

P41 ya shiga gwaji yana shekara 8 da **astroblastoma da ya dawo kuma yana ɗauke da EWSR1-BEND2 gene rearrangement**, wani rare tumor feature inda genes biyu suka haɗu. Tumor ɗin ya shafi na uku ventricle, ɗaya daga cikin wuraren da ruwa ya cika a zurfin kwakwalwa. Yaron ya riga ya yi surgery da focused radiation, sannan ya yi radiation na biyu kusan watanni bakwai kafin TAA-T da low-dose chemotherapy da aka kammala kusan watanni biyu kafin infusion. P41 ya shiga arm C, ya sami chemotherapy na rage immune cells kafin infusion, sannan TAA-T infusions uku.

Bayan ƙwararru sun sake karanta scans na kwakwalwa, an rarraba cutar a baseline a matsayin **nonmeasurable but evaluable**: tana gani isa a tantance ta, amma ba ta dace da reliable size ma'auni ba. Kusan shekara ɗaya bayan infusion na ƙarshe, bacewar non-target lesion ta goyi bayan complete-response classification na marubutan a imaging. Source bayanai sun nuna disease-free interval na fiye da **watanni 41.2 daga infusion na farko**, kuma har yanzu yana ci gaba a cutoff na 1 Janairu 2026.



Waɗannan post-contrast T1-weighted MRI images suna nuna P41 kafin infusion da kuma shekara ɗaya bayan infusion na ƙarshe. Orange squares, waɗanda marubutan binciken suka ƙara, suna nuna yankin da enhancing lesion yake gani kafin infusion amma ba ya gani a shekara 1; marubutan sun classified wannan a matsayin complete response. Bacewar lesion abin lura ne na gaske kuma mai ba da bege, amma wannan case guda ɗaya ba zai iya gaya mana abin da ya jawo shi ba: cutar P41 a baseline evaluable ce amma ba reliably measurable ba, yaron ya sami re-irradiation da chemotherapy kafin TAA-T, response ɗin ya zo da jinkiri, kuma gwaji ɗin ba shi da control group.

Wannan shi ne abin lura mafi ban mamaki a gwaji ɗin kuma a lokaci guda shi ne causal story mafi rauni. Natural history na tumor ba a bayyana shi sosai ba. Adadin viable tumor a baseline ya yi wahalar tabbatarwa. Re-irradiation da chemotherapy sun zo kafin sel ɗin. Response ɗin ya yi jinkiri, kuma babu control group.

Immune shaida ba ta cike wannan gibin ba. Binciken ya yi amfani da **ELISpot assay**, gwajin laboratory da ke gano siginar da T cells guda-guda ke fitarwa idan suka amsa ga target da aka zaɓa. Manufactured cells na P41 sun yi negative bisa original nazari rules na binciken. Positive sakamako ya bayyana ne kawai a less strict reanalysis, daga baya kuma aka cire shi saboda damuwar false positive; test plate ɗin ya tsage, leakage na iya faruwa, kuma babu sauran product da za a sake gwadawa. Haka kuma masu binciken ba su iya bibiyiing infused cells ta unique T-cell-receptor fingerprints ɗinsu, waɗanda ake kira **clonotypes**, ba. Babu sauran product da zai nuna waɗanne fingerprints ne na infusion, kuma mixed immune-cell samples daga jini da aka samu daga baya an yi amfani da su ne kawai a broad nazari, ba direct product-to-blood match ba. Saboda haka samples da ake da su ba su iya tabbatar da long-term persistence ko expansion na sel daga infusion product kai tsaye ba.

Me waɗannan immune tests za su iya nuna?

ELISpot yana tambayar ko T cells suna fitar da sigina idan aka nuna musu target da aka zaɓa a laboratory. Receptor-fingerprint tracking yana tambayar ko T-cell families iri ɗaya da aka gani a infusion product za

> a iya sake gano su kuma a auna su a jini ko tissue daga baya. Sakamako mai ƙarfi zai iya goyon bayan sarkar shaida daga target recognition zuwa persistence, amma ko da haka ba zai tabbatar cewa sel ɗin ne suka jawo clinical response ba. A nan, matsalolin fasaha da rashin matched samples sun bar har wannan supporting chain ba cikakke ba.

Saboda haka binciken bai nuna cewa infused cells na P41 sun gane targets da ake nufi ba, sun ci gaba da zama a jiki, ko kuma su ne suka jawo complete response.

P35: fiye da watanni 31.8, sannan follow-up ya ƙare

P35 ya shiga yana shekara 14 da grade 4 medulloblastoma, wani high-grade brain cancer da aka fara gano masa yana shekara 7. Zuwa lokacin enrollment, cutar ta dawo sau uku kuma mara lafiyar ya sami **disease-directed magunguna 17**.

Bayan TAA-T, takardar ta ba da rahoton dogon stability a scans ba tare da ƙarin antitumor magani ba. Source bayanai sun rubuta disease-free interval na fiye da **watanni 31.8 daga infusion na farko**. A wannan lokacin P35 ya bar binciken. A statistics na bincike, observation ɗin ya zama **censored**: follow-up ya tsaya a nan, ba tare da yin zato game da abin da ya faru daga baya ba. Ba za a tsawaita shi har zuwa final cutoff na takardar ba.

A baseline, ba za a iya auna cutar cikin aminci ba ko tantance ta sosai a scans har a classified response. Dogon tarihin magunguna da rashin randomized comparator suna sa ba zai yiwu a danganta wannan interval ga intervention guda ɗaya ba.

P36: surgery da chemotherapy kafin, targeted magani bayan

P36 ya shiga yana shekara 14 da pediatric glioblastoma da ya dawo bayan progression a standard chemotherapy tare da radiation da kuma wani investigational **PARP inhibitor**, magani da aka tsara domin toshe wata hanyar da tumor cells ke amfani da ita wajen gyara DNA da ya lalace. Tumor ya ci gaba kusan watanni uku kafin infusion na farko; an sake surgery sannan aka ba temozolomide chemotherapy kafin TAA-T.

Ba a ba da wani disease-directed therapy yayin active TAA-T magani ba, amma bayan infusion na ƙarshe P36 ya sami watanni bakwai na **CDK4/6 inhibitor**, targeted drug da aka tsara domin rage saurin rabuwar sel. Source bayanai sun rubuta disease-free interval na fiye da **watanni 51.6 daga infusion na farko**, kuma yana ci gaba har zuwa cutoff na binciken.

Wannan shi ne interval mafi tsawo daga cikin ukun. Amma yana cikin jerin abubuwan da suka haɗa da surgery, chemotherapy, TAA-T da targeted magani daga baya. gwaji ɗin ba zai iya ware tasirin kowannensu ba.

Me ya sa “bayan” ba zai zama “saboda” ba

Waɗannan cases suna da muhimmanci ne daidai saboda an riƙe iyakokinsu a gefensu.

ReMIND ba randomized ba ne, ba shi da concurrent control group, kuma bai yi girma isa ko aka tsara shi domin gwada ko magani ɗin yana aiki ba. Arms B da C sun haɗa diagnoses daban, yawan cuta daban, prior magunguna daban da expected disease courses daban; pooling ɗinsu descriptive choice ne da aka yi bayan masu binciken sun ga bayanai. Arm C ya ƙara chemotherapy na rage immune cells kafin infusion, arm B bai yi ba. Wasu marasa lafiya sun sami ƙarin therapy bayan TAA-T. Mutanen da suka ci gaba ba tare da progression ba suna da ƙaramin tumor da ke gani a farkon gwaji, wanda shi kansa zai iya shafar sakamako.

ClinicalTrials.gov da takardar suna ƙidaya participation ta hanyoyi daban. Registry a yanzu yana nuna mutane 33 a matsayin enrolled kuma yana mai da hankali ga babban safety measure a kwanaki 42 na farko. takarda da protocol suna fara da mutane 51 da suka ba da consent, suna ba da rahoton 33 da aka yi wa infusion, kuma suna bayyana manyan tambayoyinsu a matsayin safety, ko za a iya ƙera magani da bayar da shi, da wane dose ya kamata ya ci gaba. Wannan labarin yana amfani da definitions na takarda da protocol maimakon haɗa systems na ƙidaya biyu.

Babu ɗaya daga cikin waɗannan caveats da ke sa lokuta ukun su zama marasa muhimmanci. Su ne ke ƙayyade irin muhimmancin da shaidar za ta iya ɗauka.

Sakamakon **preliminary signal** ne: dalilin gwada dabarar a wani bincike da aka tsara domin estimate benefit, tare da biological ma'aunai mafi bayyani da comparison group da zai iya raba magani daga selection, timing da sauran care. Ba shaida ba ce cewa T cells sun warkar da yara uku. Ba shaida ba ce cewa sel ɗin sun ketare blood-brain barrier—iyakar kariya tsakanin jinin da ke yawo da brain tissue—sannan suka kashe tumors. Kuma ba magani ba ne da iyalai za su iya nema a yanzu a wajen research.

Me zai biyo baya

Tambayar practical ta ReMIND—za a iya ƙera magani ɗin kuma a bayar da shi?—tana buƙatar lambobi biyu. An ƙera TAA-T product a dose na farko da gwaji ya shirya ko sama da shi ga mutane 41 daga cikin 48 da aka tattara jininsu, yayin da 33 daga cikin 51 da suka ba da consent suka sami aƙalla infusion guda ɗaya. Tsarin ƙera magani ɗin ma ya inganta yayin gwaji. Clinical histories suna ba da dalilin ci gaba da bincike, amma bincike na gaba dole ya tambayi wata tambaya dabam.

Masu bincike za su buƙaci tabbatar ko sel ɗin suna gane intended targets cikin aminci, inda suke tafiya, tsawon lokacin da suke ci gaba da kasancewa, da kuma ko sakamako suna inganta idan aka kwatanta da sauran care. Haka kuma manyan bincike-bincike za su zama dole domin gano rare harms da kyau. Future gwaji da aka tsara domin test benefit dole ya riƙe bambance-bambancen da wannan phase 1 bai iya warwarewa ba: nau'in tumor, yawan cuta, chemotherapy kafin infusion, prior magani da magani da aka bayar daga baya.

Ga iyalan da ke fuskantar pediatric brain tumors, rashin tabbas ba daidai yake da babu komai ba. Dogayen intervals uku na iya cancanci kulawa ba tare da an mai da su alkawari ba. Nau'in bege mafi girmama mutane shi ne wanda yake faɗin gaskiya game da yawan abin da har yanzu ba a sani ba.

> **Bayanin edita: abin da lambobin ba za su iya ɗauka ba**
>
> Abu ne na halitta mu so wannan labari ya ƙare da kowane yaro ya warke. Bai ƙare haka ba. An gudanar da ReMIND a cututtukan da iyalai za su iya fuskantar zaɓuɓɓuka masu raɗaɗi, kuma likitoci dole su yi aiki

ba tare da sanin ko experimental magani zai taimaka, ba zai yi komai ba, ko zai haifar da illa.
Binciken ya rubuta dogayen disease-free intervals. Haka kuma ya rubuta severe adverse events da mutuwar P27. Masu binciken sun yanke hukunci cewa fatal event ɗin possibly related ne da TAA-T kuma probably related ne da underlying disease; imaging ya dace da progression. Wannan rashin tabbacin ba za a iya warware shi bayan komai ya faru ba, kuma bai kamata a juya shi ya zama zargi ba.
Code P27 yana kare sirrin yaro. Bai kamata ya sa yaron ya zama wani abu na abstract ba. A bayan kowane mara lafiya number akwai matashi, iyali da ke yanke shawara cikin matsin lamba, da clinical team da ke da alhakin kulawa a yanayin da babu zaɓi mai tabbas. Shiga gwaji bai ɗora wa kowa daga cikinsu wajibcin samar da sakamako mai bege ko “jarumtaka” ba, kuma mutuwa ba ta zama farashi da za a ce ya dace kawai saboda research na gaba zai iya koyon wani abu daga gare ta.
Ci gaban medicine ba magunguna da suke warkarwa kaɗai ke samar da shi ba. Phase 1 bincike na iya kuma tabbatar da abin da za a iya ƙera da bayarwa, gano dose domin ƙarin gwaji, nuna waɗanne harms ne ke buƙatar kulawa, da kuma nuna yadda protocol ya kamata ya sauya. Wannan ilimin ba ya mayar da wahala ta zama abin da ya cancanta. Yana haifar da wajibcin bayar da rahotonsa da gaskiya, amfani da shi domin bincike-bincike na gaba su fi aminci, da kuma tuna mutanen da suka sa samun ilimin ya yiwu.

Taƙaitaccen bayani

ReMIND wani early phase 1 gwaji ne na T cells da aka girma daga jinin kowane mahalarta sannan aka faɗaɗa su a laboratory domin su amsa ga furotin uku da za su iya kasancewa a cancer cells. Daga cikin yara da matasa 51 masu high-haɗari brain ko spinal-cord tumors da suka ba da consent, an tattara jini daga 48, an ƙera product a dose na farko da aka shirya ko sama da shi ga 41, kuma 33 sun sami aƙalla infusion guda ɗaya. Yawancin matsalolin lafiya da aka rubuta mild ko moderate ne, amma marasa lafiya uku da aka yi wa infusion sun sami severe ko worse events da aka ɗauke su aƙalla possibly related; biyu sun sami serious brain- ko tumor-swelling events da watakila suna da alaƙa, ciki har da mutuwa guda da ta cika dose-limiting rule na gwaji. A aggressive brainstem-tumor group, babu scan da ya nuna isasshen raguwa ko bacewa da ta kai predefined response threshold na gwaji. A non-brainstem groups, matasa uku sun sami disease-free intervals fiye da watanni 31.8, 41.2 da 51.6 daga infusion na farko, ciki har da complete response guda ɗaya bisa scan criteria. Follow-up ya ƙare lokacin da mara lafiya guda ya bar bincike; sauran intervals biyu suna ci gaba a cutoff. gwaji ɗin ba shi da control group, ba a tsara shi domin establish benefit ba, kuma ba zai iya nuna cewa experimental T-cell therapy ce ta jawo waɗannan sakamako ba.

Binciken ba tare da ƙarin gishiri ba

Abin da takardar ta nuna: An ƙera personalized T cell product da ke nufin tumor-associated proteins uku a dose na farko da gwaji ya shirya ko sama da shi ga mutane 41 daga cikin 48 da aka tattara jininsu; 33 daga cikin 51 da suka ba da consent sun sami aƙalla infusion guda ɗaya. Statistical samfurin ya zaɓi dose domin gwaji na gaba. gwaji ɗin ya rubuta matsalolin lafiya da suka faru da kuma dogayen disease-free intervals uku bayan infusion.

Abin da ke ba da bege amma ba a tabbatar ba: Experimental T cells na iya taimaka wa disease control a wasu marasa lafiya, musamman waɗanda ke da ƙaramin tumor da ke gani a farkon gwaji, kuma za su iya zama masu

amfani a asibiti bayan controlled testing.

Abin da bai nuna ba: magani ɗin ya warkar da yara uku; shi ne ya jawo complete response ko dogayen intervals; an nuna infused cells na P41 suna gane intended targets ko suna ci gaba da zama a jiki; dabarar tana aiki a wannan aggressive brainstem tumor; ko magani ɗin yana samuwa ko yana da broad safety.

Manyan iyakoki: Wannan early safety-and-dose bincike ne wanda kowa ya san magani kuma babu wanda aka randomized zuwa comparison group; marasa lafiya 33 masu diagnoses daban aka yi wa infusion; early signs of benefit ba su ne babban tambayar binciken ba; an auna survival daga starting points daban a ƙungiyoyi; arm C yana da infused marasa lafiya huɗu kacal kuma ya yi amfani da chemotherapy na rage immune cells kafin infusion; wasu marasa lafiya sun sami sauran therapies; cases ukun na musamman ba su fara da tumor area da za a iya auna reliably a scans ba—P41 har yanzu yana da visible disease da likitoci za su iya bibiyarsa, yayin da P35 da P36 ba za a iya tantance su sosai ba har a classified response; laboratory shaida bai iya haɗa infused cells kai tsaye da later sakamako ba; kuma fatal event guda ɗaya ya cika mafi tsananin toxicity rule na gwaji.

Yaya yawan amincewa ya kamata mai karatu gaba ɗaya ya yi? Babban amincewa ga narrow findings game da ƙera da bayar da magani da kuma matsalolin lafiya da aka rubuta a wannan group. Babban amincewa cewa documented intervals ukun sun faru bayan infusion. Ƙaramin amincewa cewa experimental T-cell therapy ce ta jawo waɗannan sakamako, domin ba a tsara wannan gwaji domin amsa wannan tambayar ba.

Majiyoyi

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