



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

## KRAS vaccine'n high-risk participants 20 keessaa 18 keessatti T cell responses kakaase — pancreatic cancer prevent godha jedhuuf proof miti

*Single-centre phase I trial six-mutation KRAS peptide vaccine namoota 20 inherited ykn familial pancreatic-cancer risk fi pancreatic cystic abnormalities qaban keessatti test godhe. Vaccine-related adverse events grade 1 ykn 2 turan, participants 18 prespecified blood T cell response criterion guutan, small-subset analyses immune persistence muraasa hanga waggaa lamaatti argan. Median 16.5 months keessatti participant tokko iyyuu pancreatic cancer hin develop godhne, garuu study open-label, non-randomized, single-arm fi prevention test gochuuf hin designed. Vaccine experimental dha; results larger efficacy trials justify godhu, cancer prevented godhame claim miti.*

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# Talaallii'n ittisa qaamaa deebii uume. Prevention ammallee gaaffii banaa dha

Yaalii talaallii mutant bocawwan **KRAS** jahaa baramaa irratti xiyyeeffate — jiinii pancreatic cancers baay'ee keessatti altered ta'u — namoota dhibee kanaaf inherited ykn familial balaa qaban 20 keessaa 18 keessatti measurable T seelii deebii kakaase. Sadarkaa I qorannoo kana keessatti talaallii-wajjin-walqabatu taateewwan miidhaa gabaafaman National Cancer Institute CTCAE safartuu irratti grade 1 ykn 2 turan: grade 1 yeroo baay'ee mild, grade 2 moderate jechuu dha; safartuu'n grade 3 severe, grade 4 life-threatening fi grade 5 taatee miidhaa-related death hanga itti fufa. talaalliin kakaafame T seelii clonotypes muraasni waggaa tokko ykn lama booda illee argamuu danda'an. Clonotype lineage T seelota shared T cell-receptor sequence'n identified ta'e dha; kanaaf clonotypes hordofuun wal-fakkaataa talaallii-reactive lineages yeroo waliin hafu moo hin hafne gaafachuuf gargaara.

Kun hiika qabu jalqabaa bu'aawwan dha. Garuu “talaallii pancreatic cancer ittise” caalaa baay'ee dhiphaa. Yaalii xiqqaa, garee tokko qofa qabu, ifaa ture; **nageenya fi immunogenicity** irratti qophaa'e, cancer incidence irratti miti. Median hordoffii 16.5 months keessatti hirmaataa tokko iyyuu pancreatic ductal adenocarcinoma (PDAC) hin uumamne, garuu selected hirmaattota 20, akka carraatti ramadame garee to'annoo dhabuu fi limited hordoffii waliin ilaalcha kun prevention mirkaneessu hin danda'u.

Kanaaf dubbisuu sirrii kutaa lama: talaallii feasibility fi immunogenicity gahaa ta'ee guddaa caalaa yaaliiwwan justify godhu fakkaata; kilinikaa faayidaa isaa garuu hin beekamu.

## Yaalii keessa eenyu scene

Johns Hopkins sadarkaa I yaalii, **NCT05013216 Cohort A** jedhamee registered, April 2022 fi February 2026 gidduutti namoota 20 hirmaachise. Hirmaattota waliigalaa calaluu garee uummataa miti. Isaan family seenaa ykn **germline** cancer-predisposition variant irratti hundaa'e predefined balaa guddaa qabu criterion keessaa yoo xiqqaate tokko guutan — germline jechuun inherited DNA jijjiirama body guutuu keessatti jiru, mutation tumour qofa keessatti acquired miti — fi hundi radiographic pancreatic abnormality intraductal papillary mucinous neoplasm (IPMN) jedhamee classified qabaatan.

Cohort median age 66.5 waggoota ture. 20 keessaa kudha torba first-degree walbira qabamee PDAC qabu turan, 12 germline variant baatan, isa guddaa pancreatic cyst median diameter 0.7 centimetres ture. Hirmaattota sagal cysts pancreas kutaa tokko caalaa keessatti qabu turan.

Selection kun barbaachisaa dha. Qorannoo vaccination monitored, unusually balaa guddaa qabu garee keessatti tolerable fi T seelota leenjisu danda'aa laata gaafata. giddugaleessa-risk people, dhukkubsattoota socho'aa pancreatic cancer qaban, ykn garee uummataa broader fi caalaa diverse keessatti talaallii akkamitti perform godha hin himu: 20 keessaa 19 White turan.

## mKRAS-VAX maal

KRAS signalling pirootiinii dha. Mutations isa permanently switched on godhan PDACs 90% ol keessatti jalqabaa driver events dha; pancreatic precursor lesions keessatti illee baramaa. **mKRAS-VAX** pooled sinteetikii long-peptide talaallii mutations recurring jahaa hammatu: G12V, G12A, G12R, G12C, G12D fi G13D. Peptides chains amino acids — building blocks pirootiinota — dha; as peptide “dheeraa” tokko tokko 21-amino-acid KRAS fragment mutant site tokko qabu. **Pooled** jechuun six pre-made fragments talaallii off-the-shelf tokko keessatti mixed, hirmaataa tokko tokkoof sequence custom build hin godhamne.

Hirmaattota vaccination rounds afur weeks 1, 3, 5 fi 13 irratti argatan. Round tokko tokko peptide pool immune-stimulating adjuvant poly-ICLC waliin combine godhe, muraasa subcutaneous injection sites karaa delivered. **Adjuvant** helper ingredient ittisa qaamaa deebii galma talaallii’tti strengthen ykn kallattii godhu; poly-ICLC mataan isaa KRAS galma miti. Lesson ittisa qaamaa sirnaaf yaadame “tumour unique person tokko recognize godhi” miti; “shared mutant-KRAS sequences pancreatic precancers keessatti irra deddeebi’an set recognize godhi” dha.

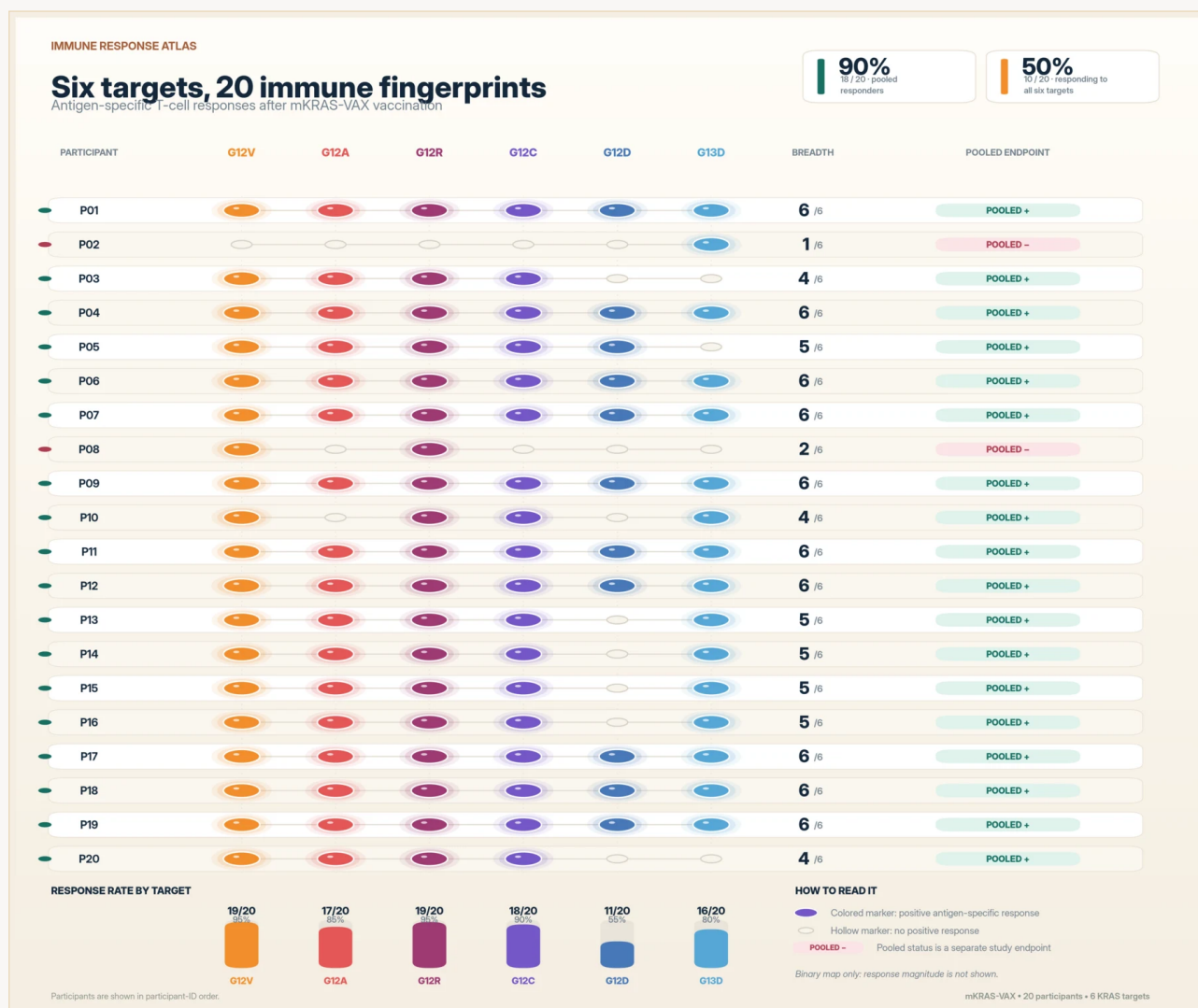
Qophiin karoorfame marsaa hunda wal-fakkaataa six-mutation, non-personalized pool fayyadame; person ykn visit tokko tokkoof redesign hin godhamne. Manufacturing caveat tokko ture: G12A peptide doses muraasa keessaa omitted ture; barruu hirmaattota four rounds keessaa yoo xiqqaate sadii keessatti argatan fi warra irraa dropped godhame gidduu G12A deebii hiika qabu garaagarummaa hin gabaasa godhne.

Yaalii co-madaallii ijoo dhumaa nageenya fi mutant-KRAS-specific T seelii sochii dhiiga keessatti weeks 17 keessatti jijjiirama ture. Vaccination cancer diagnoses ykn deaths hir’isaa laata qoruuf powered ykn designed hin turre.

## Nageenya fi ittisa qaamaa bu’aawwan maal agarsiisan

Hirmaattota 20 keessatti talaallii-wajjin-walqabatu event grade 2 ol tokko iyyuu hin gabaasa godhamne. Injection-site reactions 85%, fatigue 70%, chills 40%, flu-like symptoms 40% keessatti mudatan; barruu events kana self-limiting jechuun ibsa. Kun favourable jalqabaa nageenya mallattoo dha, guutuu nageenya profile miti. Qorannoo people 20 uncommon ykn delayed harms reliably mul’isuu hin danda’u.

Talaallii dhiiga T seelota mutant KRAS recognize gochuuf train godhaa laata gaafachuuf, researchers dhiiga seelota dura fi booda vaccination collected six peptides waliin saaxilu, IFN-gamma ELISpot assay’n responding seelota lakkaa’an. Hirmaattota 20 keessaa kudha saddeet barruu’s prespecified immune-responder criterion guutan: pooled deebii six KRAS antigens irratti 2.5-fold ol daballii. Median pooled daballii 18.2-fold ture, wide daangaa 1.8 hanga 167.1 waliin. Hirmaattota kudhan six antigens hundaaf akka istaastikiitti hiika qabu deebii uuman; even hirmaattota lama pooled responder daangaa gadi ta’an selected mutations irratti react godhan.



Hirmaattota kudhan mutation-specific antigens jahaan hunda irratti hiika qabu T seelii deebiiwwan qabu turan. Hirmaattota lama adda pooled-response daangaa gadi ta'an illee selected mutations tokko ykn lama irratti react godhan.

Original chart — The Clean Paper; counts transcribed from Haldar et al., Cancer Discovery 2026, Figure 1f CC BY 4.0

Deebii mutations hunda irratti identical miti. G12A, G12V fi G12R generally mallattoolee guddaa uuman G12D fi G13D caalaa. Qorannoo varied HLA gosootaa keessa illee deebiiwwan argate; kun shared peptide pool person tokko tokkoof talaallii custom build osoo hin godhin hojjechuu danda'a yaada deeggara — garuu mirkaneessuu hin godhu.

## “Durable” jechuun subsets xiqqaa irratti hunda’a

Persistence bu’aa barruu dhugaa dha, garuu hordoffii gadi fageenyaan deemu denominator ni dhiphata.

Hirmaattota kudha jaha optional annual dhiiga collection’f deebi’an; daataa cutoff irratti people shan qofa two-year visit ga’anii turan. Kallattii ex vivo qorannoo keessatti, 16 keessaa 3 hiika qabu pooled

deebii maintain godhan, 8 immoo yoo xiqqaate tokko KRAS antigen'f hiika qabu deebii maintain godhan. Researchers dhiiga seelota KRAS peptides waliin laaboraatoorii keessatti expand yeroo godhan, long-term hordoffii irratti tested people shan hunda keessatti deebiiwwan rehammatan. Procedure kun low-frequency yaadannoo seelota mul'isuu danda'a, garuu guddaa circulating deebii kallattiin safaruu waliin walqixa miti.

T seelii receptor sequencing amma iyyuu smaller subsets keessatti caalaatti gadi fageenyaan deeme. G12D fi G12V'f, team **putative** talaalliin kakaafame clonotypes stringent enrichment ulaagaalee'n define godhe, antigen tokko tokkoof hirmaattota sadii keessatti follow godhe. As putative jechuun timing fi selective expansion isaanii mutant-KRAS stimulation booda irraa inferred; tokkoon tokkoon receptor KRAS bind godha kallattii qormaata'n mirkaneesse miti. Median 18.6% prime-phase clonotypes waggaa tokko ykn lama irratti reactive ta'anii hafe. Kun talaallii-linked ittisa qaamaa yaadannoo muraasni persist godhu deeggara; seelota sun pancreatic precursor tishuu ga'an ykn lesion cancer ta'uu dhaaban hin agarsiisu.

## Cyst walbira qabuu exploratory dha, efficacy bu'aa miti

Median 16.5 months booda, vaccinated hirmaattota 20 keessaa tokko iyyuu PDAC ykn balaa guddaa qabu lesion surgery barbaadu hin uumamne. Kun encouraging ilaalcha dha, garuu prevention jechuun hiikuuf insufficient. Yaalii akka carraatti ramadame garee to'annoo hin qabu, cohort xiqqaa dha, pancreatic cancer waggoota hedduu keessatti guddifatu danda'a.

Investigators hirmaattota vaccinated 16 hordoffii scans qaban keessatti post hoc imaging xiinxala illee godhan. Xiqqaa cysts sadii resolve fakkaatan, sadii immoo yoo xiqqaate 2 millimetres hir'ina godhan. Resulting 37.5% reduction-or-resolution saffisa addaan assembled unvaccinated surveillance cohort keessatti 6.8% caala, gabaafame Fisher's sirrii p-value 0.01 waliin. Fisher's sirrii qormaata proportions xiqqaa count table keessatti walbira qaba; no-difference moodeela isaa jalatti, split yoo xiqqaate akkuma kana uneven ta'e chance'n naannoo 1% yeroo mudata. Kun post hoc, non-akka carraatti ramadame walbira qabuu repair hin godhu ykn association gara causation hin jijjiiru. p-value maal jechuu fi maal jechuu hin dandeenye afaan salphaatti ilaaluuf qajeelfama kilinikaa bu'aa dubbisuu ilaali.

Walbira qabuu kun hypothesis aama; talaallii efficacy establish hin godhu. Allocation akka carraatti ramadame hin turre, xiinxala post hoc, imaging hirmaattota vaccinated afur'f hin argamne, cysts disappeared naannoo 4 millimetres — safartuu fi imaging variability barbaachisaa gochuuf gahaa xiqqaa. Barreessitoonni teknika imaging dhiibbaawwan keessaa baasu hin dandeenye fi saamudaa/hordoffii ittisa qaamaa deebiiwwan cyst stability ykn PDAC incidence waliin link gochuuf limited jechuun ifatti dubbatu. PanIN lesions, precursors baramaa, routine imaging irratti yeroo baay'ee invisible; kallattiin hin safarame.

### Phase I fi immunogenicity as keessatti maal

**Sadarkaa I** jechuun qorannoo jalqabaa namaa qormaata, irra caalaa tolerability, feasibility fi

biological sochii irratti xiyyeeffatu. Prevention mirkaneessu yaalii stage miti.

**Immunogenicity** jechuun talaallii galma isaa irratti measurable ittisa qaamaa deebii uume. T seelii deebii strategy kanaaf necessary tarkaanfii dha, garuu surrogate laaboraatoorii bu'aa dha; cancer balaa gadi bu'e jechuun ragaa miti.

**Interception** jechuun balaa guddaa qabu ykn precancerous haala keessatti cancer dhaabuuf yaaluu. As goal research programme dha; bu'aa yaalii kanaan hin agarsiifamne.

## Kun maal hin mirkaneessu

- mKRAS-VAX pancreatic cancer prevents godha **hin agarsiisu**. Efficacy madaallii dhumaa establish hin godhamne, akka carraatti ramadame garee to'annoo hin turre, 16.5 months natural seenaa PDAC waliin walbira qabamuun gabaabaa dha.
- “Hirmaataa tokko iyyuu PDAC hin uumamne” vaccination irraa dhufe **hin agarsiisu**. balaa guddaa qabu hirmaattota 20 keessatti cancers eegamu gabaabaa interval kana keessatti uncertain, yaala malee illee xiqqaa ta'uu danda'a.
- Talaallii precancerous cysts shrink ykn resolve godhe **hin agarsiisu**. Cyst walbira qabuu post hoc fi non-akka carraatti ramadame, addaan assembled surveillance cohort waliin, matched to'annoo miti; vaccinated hirmaattota afur hordoffii imaging hin qabne; cysts naannoo 4 millimetres safartuu fi imaging variability barbaachisaa gochuuf xiqqaa.
- Approved talaallii **hin godhu**. mKRAS-VAX yaalii ta'ee hafa, giddugala tokko keessatti narrowly selected cohort irratti qorame.
- giddugaleessa-risk people, socho'aa PDAC dhukkubsattoota ykn hereditary-risk gareewwan hundaaf faayidaa **hin mirkaneessu**.
- Dhiiga T seelota pancreas keessa seenan, precursor seelota tishuu keessatti recognize godhan ykn cyst jijjiiramoota caused godhan **hin agarsiisu**. Adda window-of-opportunity cohort tissue-level gaaffilee gaafachuuf intended.
- Long-term nageenya ykn durability **hin settle godhu**. Muraasa harms guddaa caalaa cohorts barbaadu; strongest one-to-two-year ittisa qaamaa xiinxalawwan xiqqaa subsets fi laaboraatoorii expansion fayyadaman.

## Ragaan hammam cimaa dha?

Narrow sadarkaa I conclusions'f ragaa reasonably cimaa dha: barruu cohort hirmaattota 20 short-term nageenya daataa gabaasa godha, 18 prespecified blood-based immune-response criterion guutan, assay gosoota hedduun mutant-KRAS-reactive T seelota presence fi persistence deeggaran.

Kiliniikaa faayidaaf ragaa dadhabaa dha sababni qophii tilmaama gochuuf ijaarame miti. Yaalii milkaa'ina ulaagaalee nageenya fi dhiiga immune-marker jijjiirama ture. Nageenya madaallii dhumaa short-term tolerability irratti hojjetu; immunogenicity surrogate kiliniikaa faayidaa dha; lamaan isaanii cancer ittisame hin mirkaneessu. Absence PDAC, cyst walbira qabuu fi afaan

“interception” to’atame, longer qorannoowwan raawwachuuf sababoota ta’anii fudhatamuu qabu — substitute miti. Qorannoo investigator-initiated, tokko giddugala, immunologic yaaliiwwan muraasni hirmaattota sadii hanga shan qofa fayyadaman.

Relevant conflicts mul’ataa ta’uu qabu. Barreessitoonni hedduun KRAS peptides ykn T seelii receptors waliin patents filed gabaasa godhu; barreessitoonni biotechnology fi pharmaceutical dhaabbilee, Adventris dabalatee, waliin consulting, research ykn biraa ties gabaasa godhu. Disclosures safartuuwwan invalidate hin godhan, garuu walaba replication fi to’atame efficacy yaaliiwwan barbaachisummaa dabalu.

## Maaliif barbaachisaa dha

Pancreatic cancer yeroo baay’ee curative yaalaaf baay’ee booda argama. KRAS mutations jalqabaa arise godhu fi precursor lesions hedduu keessatti recur godhu; invasive cancer hin uumamin dura “off-the-shelf” ittisa qaamaa strategy’f galma nama hawwatu uumu. Yaalii kun jalqabaa hurdle tokko ifaa godha: xiqqaa balaa guddaa qabu cohort keessatti peptide pool severe talaallii-wajjin-walqabatu toxicity hin uumin, yeroo baay’ee intended T seelii mallattoo uumu.

Next hurdle baay’ee ol-aanaa dha. Researchers deebii relevant pancreatic tishuu ga’u, safely persist godhu, fi guddaa caalaa, appropriately to’atame gareewwan uummataa keessatti clinically hiika qabu bu’aawwan jijjiiru agarsiisuu qabu. Hanga sanaatti, kun promising immune-engineering bu’aa dha, prevention bu’aa miti.

## Cuunfaa gabaabaa

Single-centre sadarkaa I yaalii familial ykn germline pancreatic-cancer balaa fi pancreatic cystic abnormalities qaban namoota 20’f six-mutation KRAS peptide talaallii kenne. talaallii-wajjin-walqabatu taateewwan miidhaa grade 1 ykn 2 turan; hirmaattota 18 prespecified mutant-KRAS-specific T seelii deebii criterion guutan. Smaller hordoffii xiinxalawwan hirmaattota muraasa keessatti deebiiwwan ykn putative talaalliin kakaafame clonotypes hanga waggaa lamaatti persist godhan argan. Median 16.5 months keessatti hirmaataa tokko iyyuu PDAC hin uumamne, garuu yaalii garee tokko qofa qabu, non-akka carraatti ramadame, prevention qoruuf hin designed. Talaallii yaalii dha; qorannoo guddaa caalaa efficacy yaaliiwwan deeggara, pancreatic cancer ittise himannaa miti.

## Sakatta’a ifaa

**Wanti barruu agarsiisu:** Selected balaa guddaa qabu hirmaattota 20 keessatti mKRAS-VAX talaallii-wajjin-walqabatu event grade 2 ol hin gabaasa godhne, 20 keessaa 18 keessatti prespecified dhiiga T seelii deebii uume. Ittisa qaamaa deebiiwwan fi putative talaalliin kakaafame clonotypes muraasni

boodaa visits irratti detectable ta'anii hafe.

**Wanti promising garuu unproven:** T seelota kun pancreatic precursor lesions irratti faayidaa qabu ittisa qaamaa surveillance kennanii eventually PDAC incidence hir'isuu danda'u.

**Wanti inni hin agarsiifne:** Pancreatic cancer prevention; kilinikaa efficacy; approval; waliigalaa garee uummataa keessatti faayidaa; precancer seelota tissue-level killing; ykn guddaa garee uummataa keessatti long-term nageenya.

**Daangaawwan ijoo:** Hirmaattota digdama; tokko giddugala; ifaa, non-akka carraatti ramadame, garee tokko qofa qabu; gabaabaa median hordoffii; efficacy madaallii dhumaa hin jiru; post hoc cyst xinxala non-akka carraatti ramadame comparator waliin; optional long-term visits fi xiqqaa immune-analysis subsets; safartuuwwan irra caalaa peripheral dhiiga keessatti.

**Dubbisaan waliigalaa hammam amantaa qabaachuu qaba?** Xiqqaa cohort kana keessatti talaallii tolerable fi immunogenic ta'uu irratti amantaa giddu-galeessaa. Pancreatic cancer ittisa irratti amantaa baay'ee gadi-aanaa, sababni qorannoo gaaffii sana deebisuuf qophii hin ta'in.

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## Maddoota

Halder et al., First-in-human testing of a mutant KRAS vaccine for pancreatic cancer interception in high-risk cohorts, Cancer Discovery (2026)

<https://doi.org/10.1158/2159-8290.CD-25-2245>

ClinicalTrials.gov, NCT05013216

<https://clinicaltrials.gov/study/NCT05013216>