I would like to invite Dr. Simeet Suputa and the pan-nurisa Dr. Ravi Krishna, Dr. Prabhaj
Bhargava, Dr. Prashan, Dr. Dale is there, he is online.
Okay, okay. So Dr. Prashan, Dr. Prabhaj and Dr. Ravi and I would like to invite Dr. Simeet.
This will be Cheyetivas.
Welcome again. I will invite my pan-nurisa.
So now, Jean-Bhavak, for Executive GI.
So, this is a 50 year old beautiful lady with no comorbidities and on CR presentation of Abronal Distention,
and on a user I found to have also a prototype, vision and stomach.
She was fully differentiated, IHC initially showed CK positive Dx2, and how two new was actually negative, sorry.
So, PDN1 was less than one, and it was PNMR.
But she showed gastric cancer with multiple myths in Abronal node,
or mental standing by her index of masses, and the diagnosis of gastric carcinoma is test forward.
So she was started on the Firefox resume, and post three cycles, there was six cycles, there was good response,
and eight cycles of Firefox was given.
And at that time, we thought maybe NGS best testing will give us some added information, and NGS has been.
So, my question to panel, would you have done the same, or would you have liked to do the NGS initially?
We do it initially, but we don't wait for the therapy, because there is not much data, and her two prevalence in Indians in her is less.
So hardly any target is found in gastric clinically significant meaning.
In number of percentage wise, I will say very few patients get anything targetable.
So we don't wait for the, and first line approved therapies are also less.
So we start chemotherapy with respect to the changes.
And just in the special end, we found how to pause DPI by NGS, initially by IHC it was negative.
So we added Shastra's umab, and after three cycles of tests, there was progression.
So she was started in her two, also, in Tagah for, and there were the progressive diseases, after three cycles,
and she was started on an absolute nanosel and an opportunity after three cycles, she had progressive digits,
and then fall, she was started and there was clinical progression.
So, but she's still very fit.
So what next, the question is what next?
So if you see the guideline, NCC and guideline, most of this has been given, absolutely, paxxel, TDS, DOSi-textel, paxxel, and taken five of you.
So actually if we see the response rate, PFS and overall survival of this NCC and recommended,
it is around, if you, REM serumuses which we use openly is only our response rate of 3%.
And other it's around 16 to 20% and TDS, yes, in a hard to positive it has a response rate of 51%.
So she was already given.
So I think now we have very limited options.
So if there was a drop in third line or later which give a response rate of 40 to 60%
PFS of 5.8 and made in over-survivables of 9 to 14 months, what do you use it?
What do we have, blockbuster drug for someone who is not going to survive more than two, three months,
you are giving a PFS of six months.
That's actually data with this carticel therapy.
So if she was clouding 18.2 positive, the overall response rate of 14.9 and MOS 9%.
And the hard to new cartic in third line or later, 35 to 67% of overall response

rate,
overall survival of 14 to 2 months.
So with this data, now you are okay to say, give patient the cartic without any doubt.
Yes.
If I need to give you the finances as a date, then yes.
Agreed.
So in GI tumors, when we talk of cartic and Tisha, we have different targets.
Cartoon, clouding 18.2, it came in methylene, common targets.
There are many, but I have written some common.
And in Tisha, which we have already said, Keras, as asked people, Tisha are common and gamma delta.
So there are some data and some literature where even mericidic acid cancer has complete response
by clouding 18.2 cartic.
Similarly, there are mesothelene target Tisha, which has been given on multiple solid tumors,
including GI cancers.
And they have, as I have a reference, they have shown the response rate of 40 to 45%
and if you see the mesothelene target in a solid tumor, including gaseous cancer, we have median 5.6 month and overall survival of 10.6 month.
But if you see the 20 version of the patient actually survive more than 800 days, that's almost two years.
So in this patient, since it was a heart, you know,
a heart is targeting carticial was started, a phish is an infusion one turn
and she has already gone with her cartic infusion and sees under response assessment.
Next.
Now coming to another case, it's a diagnostic, so pancreatic endocarcinoma on August 24th.
And for cycle of injection, polyphenols was given.
Patients had thrombose, so the father could not be understood.
And PET CT shows pancreatic tumor with secondary lymph node, hepatic node,
and multiple bone meds.
And it's just progression of disease.
So it was T2N2M1.
So at this case, what is the next step to my panelist?
I will enroll in my ongoing trial where I'm giving GMC to Vin versus GM now, practically a second ninth therapy.
Yeah, they should have been based on third-risk.
No surgery, I'm a surgeon.
So if you see guidelines for NCC and guideline, you see that systemic therapy,
as you say no surgery, and when there is disease progression,
what option we have, we have different systemic therapy or clinical trial.
So at this time, would you love to do any biopsy in this case for any further testing?
So initially, it was not done.
If patient is of the resources, then obviously, will do a NGS testing for a patient.
95% will have K-RAS mutation, only about 5% may get something.
So in this case, a Supra-Cla biopsy was shown, and the IHC shows 99% positive of cloud and 18.2 marker.
So no other actionable mutation vision.
So you still go for the GM Stavin NAP-AC test, because I'm doing a trial, obviously.
So if you see the guidelines, many of these guidelines are based on biomarker base.
So we remove the biomarker base because there are no actionable mutation.
So you are absolutely right.

In patients who have already received five, if you base, it's usually GEM Stavin or GEM Stavin bound.
But if you see the response rates with GEM Stavin, it's 8 to 11% and median overalls are 5.7 month.
And GEM NAP-AC is 11.3% and MOS of 7.1%.
And other physician-recommended guidelines is around 8 to 10%.
So my question again is if there is a new drop by Pfizer or MST,
which on the horizon overall response rates are 54.9% and MOS overalls are about 9 months.
How do you still stick with this?
The response rate of 50% or more than 10% in the pancreas is never seen.
So you would use it if Pfizer comes with such a drop.
But actually it's a data of cloudy, clouding agent.2 based on it.
So it has an impressive record.
So these are some data for clouding agent.2.
Where even in advanced pancreatic center there was complete remission in one of the cases.
It's a case report. We won't take it as a standard. But there are reports.
So these are other reports, which are effectiveness of clouding agent.2.
So this patient was successfully under the analysis and collection of CT3 prosthesis for clouding agent.2.2.2.
So we think GEM NAP-AC is a GEM Stavin and NAP-AC is a huge data.
So he was clinical and stable and prepation are ongoing for the administration of anti-clouding agent.2.
Actually this slide was made in the morning.
So fortunately I was able to see that the infusion of gati today only.
So this patient has already got the infusion of gati.
So this is actually the gati being brought out of the container.
So next.
Is there any data of responses to chemotherapy and gati or they don't go hand in hand?
Because just four cycles of all phenoxes of poor biology disease.
He wouldn't do anything with any chemo I have no hope.
So we don't have that data.
See the data which he showed.
This was presented in this ASCO.
And the data that was in the GIS CO.
So we have limited data with 40 patients, 50 patients.
But what that is showing us is that response is beyond third line,
we are getting like 54% 60% in case of pancreatic tumors and even in case of.
In fact if you look at that data which has been Dr. Bothera I think is one of that.
It shows that even if you have a protein 18.2, if you have pancreas that response is different.
If you have a G junction tumor that response is different and even the sustainability is in different.
This case before this is actually was treated in the Romania.
And then it came from Romania to worse.
And this patient actually interestingly had his chlorinating point to positive and also has a CEA positive.
But the chlorine was present in 99% cells and was strongly positive.
The CEA was present in 70% of the cells and was moderately positive.
And that is the reason why we decided we will go with chlorinating point to Cartier not with a CEA Cartier.
But we don't have that data that after Cartier fields or in Cartier with we combine with chemo that would be what would be the A.
We had a discussion about this when we were doing Cartier should we give any chemo therapy with it.
The fear with Dr. Bhava and Dr. Bilal had an even Asha is not a bit asha has was.
If you give chemo therapy and what if it kills the construct itself.

So that is one of the fear which we had but I am very sure it will get explored in future.
So our third case 35 year gentleman no co-morbidity, ascending colon cancer, significant cell, metastatic, particular, acetyl-free and leaper.
And just source PDR1 less than 1% MSIS stable, no pole mutation and how to negative.
And if you see it was positive for TP-50 and SMA-degenerance which are not accidentable at the current status.
So this patient was started on Capiox regimen after three cycles he had progression and he was given four cycles.
And now again his progression started on task 102 vape.
PS1 patient affordable no major residual toxicity.
Your next line of action again regaraffative.
The patient is mine he has already started on regaraffative.
And most probably going to progress.
And PF is anyway 2.3 or 2.1 benefit.
This is Dr. Anup Kresser, he knows better.
So if you see NCC and guideline after fall for Scapiox.
So yeah regaraffative as you said is one of the options frequent in it and try to provide TP-plus-bape.
But if you see the response there it's around regaraffative 1% sorry to say, frequent in it, 11% and overall survival of 6 to 10.
So now we are talking about CAR-T in colon we have CA, CAR-T as Dr. B. said one of the target is CA.
And other is T cell therapy because he has TP-53 and SMA-T we have biophagic T cell TCR therapy.
So response rate 16 to 25% not as impressive as clouding 18.2 are but 16 to 25% in third line or later.
And PF is only recorded for this and overall survival are at to be reported.
So these are phase 1 trial of CA-cortical therapy.
It has been given both IV and intra-petal and intra-petal has beta-response.
So T cell therapy at the pain has discussed in detail.
So after seeing this data would you think about referring to patients for CAR-T in this such cases?
When all the treatment options are exhausted when such new therapies are available definitely.
First for the clinical trial and if not then definitely for the new therapies.
If finances are not a constraint.
Say a final comment.
Looking at all the cases presented across the different organs.
Life is very depressing for a surgeon.
That is the impression I get.
And the only hope is that the CAR-T cell therapy works well so that you can get it to an operable stage and we can help you run a trial whether the surgery helps.
So I hope the results are better and improved so that...
No I think these are options for patients.
I mean, testing for certain if we discuss about all these tests.
I know that, I know that.
So that's...
Just making this comment in a bit of jest.
That's a very good comment Dr. Kjelka.
In fact we had this discussion in ICON when Dr. Namin Khatri was discussing about solid tumor CAR-T is with us.
And one of the hypothesis he had was that many times there are trafficking issues in solid tumors.
Now the CAR-T has to reach up to the tumor.
There is so much collagen deposition in the solid tumor that the CAR-T may not reach up to the solid tumors.
So if you get response his hypothesis was Vijay you should start looking at doing

studies in which after you get a response you can you remove that milieu completely.
Question here rather than is how do you all pick up an antigen so that it can be attacked only through the tumor and not the normal cell.
Is that a challenge in solid tumors?
It's a challenge.
So if you...
The lecture on TCR you actually look at neo-intigence.
So now what happens is let's say you look at a CEA.
A CEA is expressed in multiple sites.
So if you give a standard CEA CAR-T to the patient and this was already developed in 2015 the studies had to be stopped in 2016 because of exosutoxicity.
They used to get colitis.
So today what you do is you make an armored CAR-T.
Either you would add a loss of heterozygousity variant with it.
So the loss of heterozygousity is there in the normal tissue.
So if the CAR-T sees that, okay CEA is there but there is a loss of heterozygousity it will be off.
It won't have action.
If there is no loss of heterozygousity which is not seen on a tumor then it will have action.
That is called as gated CAR-T.
So when you have antigence which are expressed across multiple sites which will be tumor and normal tissue you need to use gating.
This is the same thing and then at the end of the talk about in the...
The PSMA CAR-T actually had a good results.
But the development had to be stopped because PSMA CAR-T when you use only PSMA CAR-T in the brain they started having neurotoxicity because the PSMA expression is there in the brain normal brain.
So again if you add CA9 or you make a TCR which will be actually dependent.
So by default is actually dependent.
So if you make an actually dependent TCR it overcomes what we call as on target but off tumor action.
So it is for the CAR-T is the target but it is not what we want.
So that is the way we overcome things.
With that I would like to thank my panelists.