Thank you everyone. So the last case is will be discussed by me only or the breast and ovary and sarcoma and I would like to invite one of the most senior oncores in the town Dr. B. K. Smriti Madam. We have Dr. Sampada Desai a consultant surgical oncores is a Hindu hospital Dr. Ravi Krishna from Hyderabad Dr. Jan Gavan Desai from Pune Dr. Beringra Yada from Nepal
Dr. Pilko Puris Deh
You know like this is a exciting time in cellular therapy and I think this presentations are being made in the front of the person who has made first cellular therapy and there is no one else and Dr. Adavani sir was he is the first one to do a bone marrow transplant in India and that is the way of cellular therapy and I always still remember actually I started my career as a stem cell transplant physician and then into the medical oncology and that time one of the oncores told me why you know transplant is a dying art I said no transplant is a form of a cellular therapy only thing it is it will come in different format every now and then because what you are trying to do is I think immunity and I think it's a privilege to be present you know in the presence of the father of I will say cellular therapy Dr. Adavani sir you know who is the first type of physician way back in 1983 sir yeah and Dr. B K Smuthi Madam so with this kind of somewhat definitely you know we will see that all these cases there when we are looking at probably we have re-shined faggot so this is a CA breast you know a classical hertunu positive patient has received standards 6 TSP surgery she didn't have a patch here so adjuvant TDM was given but within seven months of TDM she progressed she has received TDX again progression in eight months desperately trying to you know give K-play again progressed in three months patient was not willing for clinical trial she was also counsel for NERAP then if took her to name but patient was not willing I think I will ask because Madam how often do you encounter hertunu resistance in a practice when they primarily or maybe it is a rare phenomena today especially given the number of options that you have so the case that you are showing is one of the less common maybe 10% falling into that group who is just resistant to everything I think within few months because I can't read properly I forgot my specs yeah so within six to seven months I mean yeah she's really very resistant to therapy yeah anyone else Dr. Birendra so how often do you encounter like Prasam as a now TCHP do we are saying you know but all cannot afford TCHP upfront but how often you see a primary trust to my pre-justice or to the resistance in your practice so very few patient you can say otherwise patient do well on TCHP
so I will not waste much of the time so basically we have discussed now some come back you know how to do this here and this is the patient was treating with the hertunu this here this was the before treatment on the left side you can see this before treatment the patient as a massive plural effusion and the right side photograph is after treatment and again this was a lever metastasis which was there which is almost around 7 centimeter within the span of six weeks this is the most reduced to less than 2 centimeters so these are something excellent responses which were seen with the hertunu cardi again this is the same patients before we can see these are multiple leverments almost they are disappearing on the right side so definitely we are having yes case selection is must and these are the expensive treatment but what I just wanted to highlight here despite of the fact you know like there's a primary hertunu resistance was there still this patient has shown a very excellent response the next case is again ovarian malignancy yes yes man the patient see she is now four months now so next case is ovarian cancer she's HRAD positive you know like now all ovarian cancer definitely we'd be doing HRAD as well as the BRCA so she was HRAD positive TP53 positive she has received three cycles of pachydaxial carboprytic surgery the hypec was done and again three cycles of pachycardo as she was HRAD she was offered ollaparip mentators but within three months of maintenance ollaparip she has the grafts which was like non-solvageable and she has received gypsidamine carboprytic plus bivasumab again progression within three cycles so

she has received then single-age and ironitic and single-age and lipodox
oral metronolary therapy and ducts on the topazid and lateral solve so CA 125
1 3 4 5 and aside this was their liver and bone meds were there patients
otherwise as a performance status of one or two so what one can offer in this
situation because she was HRAD positive actually begin with again maybe tax
and single-age and tax and pachydaxial
but there was hardly any response within six
so
polytricyptone testing is not done in India so you have to send it abroad I
think tempers is doing that they're doing combination of NGS and that so that is
one thing you can do but the drug is expensive so I don't know and I think
it's time to do NGS in these patients though we were not using it so much in
ovarian cancer but it's time to do it now I mean you might find that like in
arid 1a or something like that they may respond to immuno or give immuno along
with ollaparip so these are some of the options
yes done this has realized my bad
only had just keep you positive
only keep you positive
yeah so you didn't get RB2 on NG if you do an NGS like I have a mucinous
carcinoma the everything failed the patient even had recurrent a site is
every three weeks then we did a NGS it showed RB2 the sync amplification and
her two was C plus so in those that patient she has responded very well to
pertussumab transtrismab with chemo the site is as disappeared even the
obstructive symptoms have disappeared so so what doing NGS and then of course
the cartil you'll have to tell us because it's very experimental I know
yeah because of the heterogeneity antigen escape all these things so
it's very very investigational and I think you can use MUC or one of these
so how far you see you know there's HRD positive BLC those work put on the
arid maintenance particularly have a very short DFI very rarely less than 5 to 10
percent of the cases
so any other things you want to add?
definitely not a definitive surgery for this patient but she has liver and
bone metastasis and if she's not symptomatic and a site is the only that
is causing symptom in her we can't offer pipe in this case a few settings that
will control but since there are liver and bone metastasis it might not give you
more benefits it was only a site is then it might have been controlled with
pipe. So how many patients of CO or if they relapse you're able to salvage
you are planning like the second site of reduction I mean how many
percentage in a practice and you have a good idea?
yes we super select our patient because next of three the benefit of secondary
cytoreductive surgery is only in the setting if I can get a CC0 or R0
resection so we super select our patient to the extent of we should get at present
are more than 90 percent of our patients do end up getting a complete CC0 in a
secondary cytoreductive surgery so only less than 20 percent of the patients
which relapse must be coming on table for secondary cytoreductive surgery.
and I mean like definitely this should not be a great question but do you think
are you seeing that more of this may be as your HRD these kind of patients do
you know I mean you feel that they are better salvageable or you know they relapse
pattern.
Usually what is seen in the practices that backup positive patient they usually
relapse and they have a longer disease free interval and they are the patients
who come on table for secondary cytoreductive surgery.
So definitely this patient when it's come to the clinic she said she doesn't want
to further go very k-mutharpy or anything and whether we have also given
as man a massage serum by FC if at all we want we can do inches and she was
TP50 positive so she was treated with TCR TP53 and the dose was 4.5 to 10
rest to 7 on day 0 and day 3 she had a CRS grade 3 just in the terms of fever
chills rikers were there and she has ICANN of grade 1 with just little bit of
confusion but which is manageable. Very significant response you know

serological the response was seen on day 15 the CA-1 25 has dramatically come from 1 2 3 4 5 2 200 and almost after the fall up we are yet to deal a scan in her so I mean yesterday only I had a fall up with her and the aside this is almost resort means the the lady which was requiring a site is yes as Dr. Bikissman is pointed out you know we have to be watchful in the view that all these therapies are newer whether any escape is happening and how durable are the responses because we might are seeing this responses definitely and her scan is pending in the first week of January so we are planning the scan in the first week of January around six weeks from the time of therapy so that will know but her performance status also has improved of you know more like the fluid and everything is disappeared so she is having better at the appetite is better so let's see how she's going to respond.
You've been talking of so many targets for these cellular therapies now P53 happens to be the most frequent in most tumors and I think this is off the shelf right yes so this is the off the shelf is the prepared one yeah so this is basically when these are the patient specific this is so we did the biopsy of the tumor and then we take the T cells from the tumor from the patient's blood we send to the lab they prepared it they do the again analysis that human and it's a patient specific these are so how long four to six weeks around six weeks it took for the patient so meanwhile we have just given one solid wage regimen in that I've just given a like what I've been one cycle which was given and four weeks gap was given and then the trauma.
So last one is a 26 year old male alveolar softwarts sarcoma left eye with lung mates he has received I-fos doxorubis in progression within four months he has oral metronomic in the terms of panzopanin again progression in three months gem docet axel again progression in two months on NGS there is no actionable mutation no probate I think like we have a smart specialist how often you have some targeted mutation in sarcoma when you do NGS so many very rarely this particular pace I wouldn't have send NGS also any because I know it is a SPS then there will be a transfusion of the TFE 3 genes so nothing would have come on NGS otherwise also so I wouldn't have sent it. So basically young patient so what will you have options because he is otherwise we can find because sarcoma most of the times we realize you know we're giving therapy of the therapy probably what we are having the best response rarely partial response but most of the time stable disease patient is well maintained become with the scans now progression what I have started giving so not enough with combination of neural map for a SPS because there is some data for immunotherapy till now they have to be presented at Delos conference two or three patients my resident one first price for that is it great you are taking this as I said this unit anyway as far as we get and it's one of the worst sarcoma to have because it really doesn't respond to chemo so I think one can you directly to synitinium and then this is some good data that he is saying that could combine it with immuno because as as immuno alone it's not responsive so I think the combination like in some other two most TKI with immuno
Genes are you take one sarcoma you know like I'm not saying here but how many times are really in
different sarcoma we see a targetable mutation you know working very very very very very very very
your experience clearly this sarcoma is the corresponding beta to immunotherapy most NART you can give immunotherapy and there is good response seen compared to only NART alone so UPS and is UPS and MBS are liposarcoma
so most of the times we land up in this situation
sarcoma these are the patients who will be otherwise will be there and you know you don't know actually what to do again this patient come with this and this is autologous T cell therapy for a major a for sorry cancer in HLA 0 to patients which is a phase 1 trial and that's a show on so this there's a near and complete so this patient is received so there's a near and complete metabolic and morphological regression of the neopratic soft
illusion in the lower thigh muscles there is reduced activity also

sclerosis of this significant degrees in the metastatic bilateral non nodules and residual so this patient is now three months forced therapy let's see like how long this therapies are remaining basically because as madam has pointed out you know we are this is something which is investigational so definitely we cannot push for but when you are actually cornered maybe we can offer the patient but till our time will tell us how durable these responses are going to be because I think we were a tender lecture you know they have said he this is a one-time therapy you know as compared to when we are saying the standard immunotherapy and other things but I think there are certain scenarios where I think we get to explore but only thing is that this exciting time in the immunotherapy bracket I think this can be just one of the arbitrary I would just like to have like one one final comment from our
agreed adding one more armamentarium is beneficial as I was there as a panelist in GI also or in this such cases where via in solid tumor it used to be that we are doing palliative therapy most of the times so even if it adds some years months or years to patients life it is useful whether it will have a long-term response that time will say but even right now few months or years that we I've learned today is beneficial
well at least in Gynak malignancies as I said ovarian is investigational but it has been approved for cervical cancer so I think that's where you have to see and of course endometrial it would be investigational because you already have immunotherapy and immunotherapy combinations and in breast we have so many options so I think it would come much later down the line and maybe more more in her too positive and in those small subsets who are you know resistant so I mean that's where I would place it I mean any worry or you do you feel any safety signals will be there in the future like you know most of the times when we are using this therapy second malignancy or anything like that in which condition ovarian cancer you know I'm saying he using this cellular therapies leading to secondary malignancies well you know when they have already received several therapies we really don't know whether the incidence of second malignancies due to the multiple lines of chemo or the cellular therapy to be ever difficult to this I mean it happens with ovarian cancer use ollar perip down the line way initially previously so they said increased MDS this thing but was it due to the multiple lines of chemo or just due to ollar perip it's difficult to see some of the uo ticosilative different it is wrong to ask for surgeon but still I think it is worth it in trying in patients where all the lines of chemotherapy have exhausted and I hope it starts working especially for what do you so yes this cell
or therapy is emerging so yes if you have you have finished with everything so you can still try and let's see the results how it will come yeah yes and definitely when all the options are exhausted and finances are not a constant definitely push further you know fingers crossed right now we have to wait for long-term data but definitely you should keep it in your mind that this could be an option so all the recurrence is a intra peritoneal so yeah are you looking at some sort of cellular therapy which could be introduced intra peritoneal like you said in gbm you give intra ventricular so I think that is one thing should be explored in ovarian cancer because even the most recurrent it's very rare that you get metastasis some right mainly intra peritoneal so your
my point is very well in fact in gbm intra-carrutary has come and so they have started exploring it in CEA Carti CEA Carti's CEA Carti's have been explored in troponibut we don't have up till now is one data of someone exploring this Carti's in the ovary but what your point is correct it will come definitely as we get more about this
yeah it's point well taken yeah I think thank you thank you very much panelists and I mean we cannot like end this I think I want like final comments from the father of cellular therapy in India yeah well I think the whole whatever we have listened today and whatever we have been looking at it it appears that just like initially we had surgery radiotherapy and chemotherapy then we got the two therapies target therapy and the immunotherapy and they were really

transforming transformation in the mental treatment of the cancer and now
I think the therapy is going to come the whole area that how we can target the
tumors in the subcellular fraction I think that is what is important it's not
only the surface protein or what is there inside also focus I think say
exciting time the data more data has to come and I think once the data gets
consolidated I'm sure there's still become a sixth standard treatment thank
you so there are a lot of students in the you know so just understand this workshop
was just a exercise to what are the newer happening that is standard to do not
write the paper that I will send this patient for adaptive therapy or whatever
so the most important thing is that we should know you know what is happening
so this is not so even if you look at the incision guidance these things won't
be there but you should know what is happening around you know it is not you
know like because you always say you know like if you are just concentrating
because now I think the era has changed but this will be an exact question in
example
so think is that what we are discuss all these things where you are absolutely
put it under the patient's lecture is most important again as a senior
author is like Dr. B. Kismatam is saying sorry Cinkey we need a more data yes
definitely how the data will be generated we're treating more and more cases and
we are getting more and more confidence definitely but we have to look at all
the standard therapies we have to understand the biology definitely this
is a new beginning but get to get a lot of data and I think the future is only
thing is a brighter in the terms of cellular therapy and maybe you are just
slowly moving away but that doesn't mean that you know chemotherapy is gone
forever it's still there still standard of care in
the middle therapy has come as a now we are seeing you know different like
you know head and neck is there or lung is there it is coming the neo-adju
and setting one breast triple negative we're using neo-adju and immunotherapy
so I think it is going to change a paradigm shift but still then I think we
have to remain updated thank you very much thank you just two last questions
one thing is what is the cost factor involved now since you're doing it in
India and you know you're getting the source from local sources so I just
want to know what's the cost involved so we're going to answer that
I'm at that it is not coming from local sources our GMP manufacturing unit has
has started building up by June or July we would have the inspection from DCG and
then the manufacturing will happen local at present we have partnered around 15
labs globally so the the BCMA comes from California for us a few of this
come from Caltrans, from Visburg, Germany few of this come from Israel few of this
come from Beijing few of them from Zangzhu few of this come from Malaysia
few of this come from Singapore so the cost completely different from which
lab it is coming the cost can be as well as 50 lakhs it can go up to 1.2
CL depending on the hardware sending it across the Atlantic is very costly and
getting it across the Atlantic is very costly and how many is the cost there's
an import duty on it and this is a GST on it so the product cost skyrockets but
the thing is I had actually initially when we had council I'll tell you or
store some of the patients option was to do this here the option was to do this in
MD Anderson in a clinical trial in fact I told him you do it here you will have to
spend around 70-80 lakhs why don't you do it the patient took it to once and
actually scored it like anything the patient ended up spending one point it
began in MD Anderson till he reached the clinical trial itself that much money
was exhausted and medic staying expenses and everything were others but we feel
that once the manufacturing starts here and there are clinical trials we are
waiting for the DCJ to give us the clearance for that after that I think
the cost would come down substantially down in India etc. So I think in solid
tumors as opposed to hematologic malignancies I think that duration is
very important I know that we are offering it way down the line maybe a
little ahead it may work better till we have the data of actual what is the
median survival or even I don't know whether we can talk of PFS and what do
you say from the experience in solid tumors till now with these type of pieces

is it just you know stable disease can you talk of PFS now?
I have till now we have done 48 cases the reason up till now we have done 40 cases but the we started only in June ma'am so it is not even 6-1 and that's the reason why we did not show our data we have analyzing our data and you will be seeing we are presenting our data in ASCO this year which will be for I can and but for the survival outcomes we'll have to wait for the end of 2025 to come I think that is the time things will be more mature to talk about this point of like any phage one therapy the response rate maybe the target and point at least for that so the only thing is that when the options are and the thing in patient want to do something for that at this point of time they have to go outside search money so at this we have an option and those who can afford knowing the integrity of the subject that options are limited it's not various amount of care but some wants to try at this we can have an option in India to send those patients