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ndocta dippali bagilisia randocta George online.
So good evening everyone.
Now we will be discussing about these rasek tumours.
So, starting first with an isopasial case.
So, he is a 60 year old male patient, hypertension for the last 15 years.
No history of surgery.
He was diagnosed with scomasial carcinoma of the isopagas with liver metastasis at presentation and March 2023.
At baseline, he has a CPS of 2 or 2 negative and there was no other target mutation.
He was started on pachyletaxal, gabu platin and nibuluma.
Post 4 cycles, significant response was present.
So, completed 6 cycles of the same regimen and then continued on pachyletaxal and nibuluma for 2 more cycles.
But patient progressed and the treatment regimen was changed to vivacism, plus nibuluma.
Post 4 cycles again, there was disease progression and the liver changed to anotic end plus nibuluma up till February 24.
Then patient received gymsit, a mean plus femoralism up till April 24 followed by S1 therapy.
Then he also participated in a phase 1 study at Tata and had a progressive disease and then was given task 1 which again the patient progressed.
So, he had almost within 1 and a half years, patient have received multiple lines refractory to all the regimen but maintained performance status.
So, usually locally is controlled but the liver was started with disease.
So, just would like to ask whether you again consider for other line of therapy, chemotherapy or what will be your treatment approach in such patients?
Nothing much to, we already cost 4 to 5 drugs within 1 and a half years and I don't think any further conventional therapy might benefit this patient.
Since the PFS and OS like PFS is very less after each therapy.
But the patient performance status has maintained and they are doing for you.
No, no, so we will even it for synodic therapy.
There are people but no conventional therapy per se.
No conventional therapy.
I agree with Indakrano.
I think at such situation we don't have much data and much response with any of the therapies.
So, we will see what are available especially for you.
Just non-affording I would be challenged with the tax in or maybe not packet tax in that is the only thing what I can think if it non-affording.
I always say that in this situation the generic chemotherapy drug which you have not used it we go back sure cellotherapy is a immense option and I am never saying no but majority of the time you will end up having.
So, see your list I do say keep taking which you have not used and we end up using again repeat for me the question remains has a safety been there or not.
Good thing is that for most of the chemotherapy safety data is there because they have all been tested in face trials in various settings earlier and then you choose one of them be careful using it see that patient doesn't land up in ICU till you do that.
So, when we talk about the second line as I was saying that taking so we have so many options but in this patient all of them are exhausted we have used the immunotherapy the single agent chemotherapies and the combinations also and these in not any of the markers were positive for NTR or MSI.
So, as we see also the progression free survival is only 2 to 4 months on the success of line of therapies and such patients.
So, this patient was given the option of gamma delta infusion as patient can afford to he was started on this therapy he received this therapy every 2 week patient tolerated at well with a cytokine release syndrome of grade 2 fever of grade 2.

So, as extensively discussed the you know manufacturing and administration of gamma delta decils.
So, we have various ligands also in the various locations for the solid tumors that can be targeted with search therapies most common being the MICA and B and ULBV13.
So, as we can see the response the patient has a beautiful response with gamma delta therapy and the initially the liver was started with metastasis which has responded after treatment.
So, when we talk about the other therapies also and the targets in the solid tumors so we have GPC 3 ICAM-1, ROR-1, CAN, Nizothelin that can be used in the various tumors.
So, and these are the mutations and the genes and can be targeted with these therapy that is the Keras G12V.
So, when we talk about the data that is available so the recently a data was done in which they have used a GPC 3 targeted CAR-D therapy in the hepatocelar cancers and that can be expressed in the chromosome of the lung also.
When we see the response rate only 1% progress and there was a significant response to the therapy and many of the patients they have an objective response rate with them.
So, when we talk about they have included around 22 patients and in which 50% of the patients have partial response to a treatment.
So, and 91% of the patients have tumor reduction which is a very good data.
The same it was published in the NGEM in which they have targeted DLL3 by specific T cell engages for the neuroindocrine cancers and they have seen that the median duration of response was around 9.7 month with an objective response rate of around 40% in the patients.
So, it is a future with bite as we were discussing earlier also you need multiple lines of therapy and with each line there is a risk of having serious adverse effects also.
So, now they are coming up with a future way to avoid the need for multiple transfusion and to have a sustained effect with a single infusion only.
So, for that there are different generation of research that have been going on to have a continuous secretion in the patients after the initial single line of therapy.
So, as we can see there are various antigen that have been detected in the various.
So, even in the solid tumor also DLL3 bite has been seen like in small cell lung cancer also with many of the patients having you know beautiful response with one patient having a CR also on these line and most of these patients they have received multiple previous lines of therapy.
But still the patient is having 30 to 40% of the objective response rates with these therapies.
So, coming for patients with the Keras mutated mutation and pancreatic cancer. So, this was a study that was done in 2022 and it was applicable to lung cancer also and the patient responded with the Keras directed therapies and these patients.
So, this was the patient 73 year old male non small cell lung cancer who have a mutation in Keras G 13 V mutation was present.
Patient have received Pakli Kapo Nevo EP had a progressive disease and received dosy taksal Ramishwana Ma. So, he was given the option of Keras TCR and the patient had under one therapy and the response assessment is still awaited in this patients.
So, as previously discussed with us so, all these complicated patients in which we have you know refractory disease post multiple lines still maintaining the performance status.
So, if patient can afford it. So, definitely this is the way to go now after next thing after immunotherapy and these patients should be given an offer if they are affordable for it.
Thank you.
Is there any chance of graft failure when we infuse gamma delta because we are giving exogenous cells from other person.
So, is there any market or monitor whether what is the efficiency what is the level

of gamma delta which is maintained after one week to week.
So, T cells basically you have two one is alpha beta and one is gamma delta. So, alpha beta is HLA dependent while gamma delta is HLA independent.
So, that is the reason my gamma delta T cells usually do not cause there is no rejection.
So, there is no like GVHD or anything. The other thing is that if you really look at gamma delta actually it started from autoimmune disorders.
It is the primary use you still study I mean like if you look at gamma delta the primary use always has been autoimmune disorders.
It is only when we are now saying it is immune modulation and other things which are actually in the key role in that you want microairmen and that is where it is coming into play.
So, not that I really understand much awarded but what are the age criteria for recommending like is it okay for a 70 plus is side effects less than.
Yeah. So, yeah. So, these are actually do not have much of the side effects basically see the things that is just require simple conditioning.
Usually gamma delta infusions the first time in fact we keep added beta patients maybe for three to five days.
Second time on what is you know because gamma delta is allogenic. They have six infusions every alternate week.
So, other once it is tolerated actually it can be given like a daycare basis.
But if you look at you know like if I have to compare CART and TCR and the gamma delta is gamma delta is less activity as compared with they are not too specific.
We are looking at immune modulation the cytokine up regulation you know suppression of the T-ray and other things.
We are looking at the different things but when we are doing it more targeted manner like you know Keras you have T-P-53 you have Hartoonyo they are more specific.
But yes they have to be engineered in those patients where you know like in this kind of patient you know I developed a 7580 the only advantage with gamma delta they are of shelf.
And because if you have to prepare CART or TCR the patient needs to be very fit because they have to undergo a Pharisees the cells will be collected then tumor tissue will be biopsy done.
And you know the entire process takes around around 4 to 6 weeks plus response is better another 3 to 4 weeks.
So, we should have you know good patient GC for at least 10 to 12 weeks actually before you offer them.
Sir if patient has any active baseline autoimmune disorder like constative colitis or any other autoimmune rheumatitis.
So, can we give cellular therapy or there is a like ICIVS or some sort of medication.
So, that same thing the gamma delta first use was autoimmune only.
So, it was used for that autoimmune.
So, if you look at the maximum differ.
Yeah, also it is colitis was that that is why I want it.
Thank you very much.