Metabolites in various the micro-garisms in the microbiome.
I think because we are running short of time, I will move on to the panel.
I would like to introduce our moderator, Dr. Ajay Singh.
He is a medical oncologist at Medanta Lucknow and will invite our panelists.
So Ajay will be moderating a panel based on all these abstracts that we discussed in the
past session and I would like to invite our panelists, Dr. Subhana Rao, who is a medical
oncologist from PD in Hinduja Hospital Mumbai.
Dr. Anupto Snaivan from Aurangabad.
Dr. Ravi again.
Ravi join us back.
Dr. Harsh, Dr. Shavam Singla and Dr. Sinhit Sapkota, who is a medical oncologist from
Nipak.
Please join us on stage.
So, good evening everyone.
I think except for Dr. Siamh, we have all the panelists here.
So, just now we have a discussion regarding the metastatic non-small cell lung cancer
which are gravimutation negative and the role of various recent advanced newer molecules
in metastatic NSC, which are gravimitation negative.
So, we will have a short panel discussion on same.
So now, in today's era, how do we optimize the therapy in individual patients?
Not only in lung, but again in breast cancer, renal cancer.
Mr. Nao, what are the newer methods to optimize the therapy in advance when we come to the
systemic therapies?
Dr. Harsh, or Dr. Ravi, you can go ahead.
Yeah.
So, it all depends on the like especially in lung depending on the histologies.
So, whether it is like a squamous or adenol or like a small cell and second thing depending
on the biomarker status.
So, whether it was coming as like positive or negative and these are the things which
we will decide and depending on the disease burden of the patient whether she had like
whether she is really symptomatic for the disease or just like an asymptomatic metastatic
disease and the general condition of the patient.
So, these are the four things which I would consider before starting any line of therapy.
So, anyone wants to add anything?
So, yes definitely nowadays not only the issue of means we take care of all the factors
like patients fitness and for stability access to the accessible drugs.
The main factor is the now we have moved ahead from the histology based on biomarkers
and lung is the prime example where we have learned how to utilize the therapy for individual
patients in different scenario also means extra protein from lung to the breast cancer
patients renal cancer patients we know the now different molecules and different drugs
available in different scenario.
So, coming to the NCLC so, these are the different broads spectrum of drugs available

chemotherapy, targeted therapy and checkpoint inhibitors which has specialized targeted
therapy and checkpoint inhibitors which has changed the outcome in advanced lung cancer
patients and we do a basic biomarker testing and divide these patients in different groups
whether drug or mutation positive or drug or mutation negative and less importance is
right now means still there is importance of non-scharmulants, commerce but if any
patients come to the recommendation negative or can take immunotherapy drugs though so
histology is not that much significant.
So, what percentage of your patients are the recommendation positive in your clinical practice
in current era?
Dr. Harsh.
So, I think 30 to 40 percent of patients are driver method positive the prevalence is
more in patient when women and non-smokers.
Super number.
I think I would agree around 30 to 40 percent we live in EJFR.
Anum sir.
My practice it is roughly around 50 percent are positive.
Yes 30 to 14 my practice.
Okay and coming to the pediatric positive irrespective of whether they are rare mutation
positive or negative means how much percentage you see a pediatric positive in non-clinic.
So, overall if you go to the some data which was presented for TMS from Kumar sir and team.
So, they have shown that in Indian population almost the EJFR positive little bit higher
it is around 23 to 25 percent up to 30 percent it was only 15 percent in European population
then these are the based on the previous methods where we used to use more majority of the RTP CR the based method ISC based method.
But nowadays in our practice we are more of a kind of using NGS based testing and nowadays
we are seeing these may be these positive rate is gone little bit higher may be EJFR from
15 to 20 percent I think nowadays we are seeing more of EJFR and ALP another rare mutation
which were used to say that in red and raw based on the NGS testing more and the EJFR
by exon 20 insertion based on the NGS now more and more number of patients are able to get diagnosed with this and may be if once the updated data comes based on the NGS testing
these number will become higher where the mutations are on higher side.
Similarly the PDL1 testing so based on the historical data from keynote 0 0 1 keynote
0 1 0 and 0 24 almost 67 percent of the population were having at least PDL1 positivity and out
of this 28 percent had PDL1 more than 50 percent.
So this PDL1 marker is one of the predictive biomarker for immunotherapy so and this was
the data by the title in 2019 in lung cancer where they from near world this express study
they have shown that among 2300 plus patients the PDL1 positive was around 52 percent who

had more than or equal to 1 percent PDL1 expression out of this around 22 percent had PDL1 on
more than or equal to 50 percent and across the globe between euro or Asian American they
have shown these rates were almost similar so almost 20 percent population 22 22 had
PDL1 more than 50 percent and half of the population had PDL1 at least more or more or equal to 1 percent. So so if you exclude the diagram mutation positive become directly to the
diagram mutation negative population and those dermatologist negative patients are now treated
based on the PDL1 positive whether it's a more than 50 percent 1 to 49 percent or less than
1 percent that is PDL1 negative. So coming to the first subgroup more than 50 percent so
Dr. Nupsa what is your first preference in this population whether you will go with immunotherapy
alone or still you use chemo or immunotherapy combination. I would prefer immunotherapy alone
if immunotherapy alone is more than for PDL1 50 percent I generally prefer. Some patients if
I find that the disease burden is high chances of resistance would be more and then I add a
kibupla psi. In young patient and in a disease burden very high I add chemotherapy to immunotherapy
otherwise it's immunotherapy alone especially in. So I agree any subgroup where even though it's
more than 50 percent you refer to you chemo immunotherapy. I agree I mean a huge disease
burden you want a rapid response you start with chemotherapy anyway and I add immunotherapy.
I did read that some patients with STK 11 or KEEP1 mutations patients or females not
you know smokers even though the PDL1 is very high there there is a clear cut benefit of
adding probably there's it's suggested to add chemo with immuno. There will be more than 50
percent immuno definitely with chemo in case it's a huge disease burden.
So yes so as I said like more than 50 percent immunotherapy is yes but combination of chemotherapy
has improved the response rate but it has not added any survival advantage. So as mam said like if
the patient has required any response immediately but bulky disease which organ compromise in those
patients yes we can add some chemotherapy but otherwise immunotherapy alone would be more
than sufficient. So I also agree in majority of the cases when there is a peer advanced stage this is
diametersin negative and pediatrician more than 50 percent. Now we have sufficient data to
consider immunotherapy alone and there are different molecules either bembraszumab or
combination of nemoepi and few Chinese molecules are coming on recently lost taro parimap
and fewer in pipeline maybe immunotherapy alone will be the sufficient therapy in this
subgroup but maybe a time will come where patients in having a significant disease burden in terms of
bony mates or lung mates where we need some rapid response. So only for those those

patients
who need rapid response we can consider adding hematia otherwise by and large more than 50 percent
immunotherapy one of which are molecules accessible will be sufficient. So this is the
fire data from keynote 0 to 4 where you can see that there was almost 32 percent of the population
had was alive at 5 years compared to 16 percent in the placebo group. So even in this group also
there was a significant number of population more than 40 percent who had crossover and took
immunosurpetal despite this almost there is a doubling of the overall survivor at 5 years
and also the median OS improved from 13 to 26 months. So there is no doubt in this population
based on this keynote 0 to 4 and other molecule for atisulism map and neole map.
Whenever there is a pteron positive more than 50 percent we can consider giving
immunotherapy alone. So for this similar population recently we discussed one at Galaxy
lung 201 study which was phase 2 study in which diastodal map added bell rest root root. So in
this the diastodal map they have where we I think for whatever whoever doing this trial for
this drug they are choosing very widely the most suitable population whether it is a
co-orectal or endometrium where these drugs are approved. In similarly in lung they have
compared the docirally mav with femulismav in parallel study where they have found
the outcome was almost similar whether it is a response rate or PFS or OS. So to improve the
outcome further they consider adding a bell restotac which is the anti-tigid drug.
So in this so this is a phase 2 study and they have give a kept bell restotac in different
doses to 100 and 400 and 1000 mc. So the first primary outcome was the overalls response rate
and in this they have shown key the overall response rate was almost double from 35 percent,
37 percent of ranging from 63 to 76 percent between the different doses of bell restotac added.
So primary endpoint at this short interval around 7 month or 6 months follow they have shown
key it has made the primary endpoint. But still we need better data in terms of PFS and OS to
to see whether this response rate will convert to effective survival outcome.
And another point is that best result is one of the anti-tigid molecule and recently there was
update from Merck where another anti-tigid molecule like with Y-Bose-Trolumab anti-lactic molecule,
favivazulumab they have removed from the market because in this QY03 QY0074 NCLC then QY0064
small cell lung cancer and the for key form 008 they have made the fertility endpoint and
have not shown any significant benefits. So all these anti-tigid and anti-lacti molecule
from Merck has been withdrawn from the and the studies were discontinued. So I think at present
other than NTP D L1 and CTLA4 we are there to find the effective immunotherapy molecule.
So coming to the another subgroup PDL1 1 to 49 percent. So these are the different

combination obviously in this subgroup immunotherapy alone is not preferred choice we go ahead with
the combination of chemo immunotherapy. Anyone of you consider giving only chemotherapy alone or
to avoid chemotherapy?
No sir I would like to add immunoplascry more rather than giving single agent.
So regarding this also again we had one recent topic discussed today's by speaker on the I1
C map versus chemotherapy map in PDL1 positive advanced NCLC that is harmony 2 study. So I1
CMA is basically a dual blocker which inhibits PDL1 as well as the VEGF marker. So in this
they have shown when they compare the feminism alone against the I1 CMA they have shown the
primary endpoint PFS was significantly better and the overall response rate improved from 38.5
percent to 50 percent and the disease control rate improved from 70 to 89 percent and in
different subgroup like PDL1 1 to 49 percent or more than 50 percent this responses remain
same. So primary endpoint PFS remains significantly improved in the I1 CMA and again irrespective
the histology is commerce and non-scomas this I1 CMA molecule has shown significant improvement
over the feminism alone. So I1 CMA is basically a VEGF plus PDL1 emitter and similarly we have
ABCP regimen. Here they have given four cycles of or six cycles of chemo along with the
blue bivar cymbia and atisolism map. So suppose both these molecules are available so what will
be your difference whether you will go with the I1 CMA about atisoplast biocombination.
I1 CMA model preferred we have can reserve the tax tax aid and platinum for later line also the
hair fall that issue is there and then we have to compare obviously that OH data and the toxicity
also but then we can keep the tax reason for the like.
I think that the trial that the PFS with just pembrolizoma was just around five months which is
kind of little surprising it's similar to how much we get probably with a chemo combination
upfront otherwise yes a chemo free regimen would always be preferred.
Okay so four meals are present we are a very early stage for I1 CMAB only based on the PFS
and some response I think I will hold on we have proven ABCP regimen is in combination of
PFS map where they have shown adding bivar cymbia to atisolism map has definite statistical
significant improvement in overall survival compared to giving only bivar cymbia or atisolism map.
So I am following 150 was the multi arm study where they compare the different arms and out of
these the combination of bivar cymbia and atisolism map has shown significant statistical PFS as well
as OH advantage. So coming to the last group PDL1 negative so anyone you prefer to add immunotherapy
chemotherapy negative PDL1 negative marker in this subgroup. Yes definitely so like so though it is
PDL1 is negative it is not a perfect marker so my thing was like driver mutation

should be negative
for adding immunotherapy to the chemotherapy or not so that should be it I would think in those
terms only rather than taking the PDL1 as a strict biomarker yes if it is more than 50 percent then
I would definitely consider to strict to only immunotherapy alone or adding chemotherapy to it
but if it is less than one percent that does not mean like the patients will not add and will
not have any benefit there are multiple trials are also there like sigma 9LA so you can add
double immunotherapy along with the chemotherapy or like IO IO plus chemo or IO plus chemo yes I
would definitely consider immunotherapy even if the PDL1 is less than one. I would love to see
with it at your place. I agree with him earlier you if it is less than one percent we used to
avoid immunotherapy but now there is data and as you said the PDL1 is not a perfect biomarker so
we are adding more and more along with chemotherapy. So right now again for PDL1 more than 50 percent
and 1 to 49 percent there is no doubt immunotherapy had the life to the patient but even in PDL1
negative subgroup also now we have seen this pooled analysis presented by Dr. Sowaz Agresar
have shown key in this they included four population from keynote 189 keynote 407 one
Chinese study and one Japan Japanese extension. So in this they have shown over 5 years there was
a some improvement in overall survival from 9.3 percent to 12.5 percent which is statistically
significant and the median OS was from 11.4 to 18.4 percent. So even though PDL1 negative subgroup
is a very poor biological group but still in this subgroup also if you add able patient can afford
and you are able to give immunotherapy definitely it will add life to the patient. So obviously the
magnitude of benefit with immunotherapy is higher in the PDL1 higher group moderate in the PDL1
1 to 49 percent and lower in the PDL1 negative group but in all subgroup immunotherapy has shown
it had give some benefit in terms of saving more life through the patients.
So these are the different newer immunotherapy markers like 3 digit TEM3, VISTA, B7, S3, BTLA
whether studies are going on out of these mark has withdrawn to two or three molecules which are
targeting TZ 10, LAC3 because they have not made the they have made the futility endpoints so that
they have to withdraw these drugs like QY003 and 008 and 006. So one more article we discussed
today is the relative retry map incommensational in neolumab in relativity 104 study. So here they
have given the combination of neolumab plus retry map incommen- plus doublet platinum base therapy
along with alone neolumab and double platinum bed surface. So in this phase 2 study the primary end
point was the overall response rate and in intensity rate population there was not much
median PFAS was not significantly improved it was from 6.0 in the neolumab alone

and the 6.7
in the neolumab and relam and the overall response rate improved from 43 percent to 51 percent
difference of 7.6 percent which was not statistically significant. So overall it was a negative study
but in the subgroup analysis they have shown which was pre-specified they have shown those
population who are expressing PDL1 and non-scombus the PFAS was improved in this population
as well as the overall response rate. So again this Rayla is the
anti-lactery anti-monoclonal antibody so whenever you are making more mature data is available so we
need to choose the population very selectively. So in the future we know this drug is available
we need to check the mature data and maybe based on this data only the patients who are having
PDL1 expression or non-scombus histology will be considered any comment from your end.
I mean as I guess NIVO EP which works even in PDL1 negative this particular combination did not
work in PDL1 negative. So that is the only thing so I do not think always combination of two
you know even a therapy agents will benefit we still have a will have to probably identify
specific biomarkers to see which will work in combination.
So I think this is a dual means this concept will be like dual enthi-immono therapy drug like
3 and PDL1 and again overall it is not very much positive study but at least in the pre-specified
subgroup PDL1 positive and non-scombus they have shown there is some benefit and maybe with more
mature data we will get some more information and may adopt this in clinical practice.
So most important is the loaders versus standard dose immunotherapy which was discussed today.
So obviously this loaders has shown at least it is non based on this in terms of overall
survival and progression fee survival is non-infrared to standard dose.
So I think these studies were planned we mean I was also in TmH we co-marcer has planned 450
mg 3 weekly dose so main main issue was the accessibility to the immunotherapy drug where
major tap our Indian population was not able to take standard dose therapy but now over this
coming last two or three years the companies the pharma companies has changed their pipe support
and now almost I don't know where these loaders immunotherapy concept will lie.
Akil Sahir is there.
So this regarding loaders means how now excited you are regarding giving loaders immunotherapy
to our patients.
So I think the loaders that grow but not giving as a till now because while it is coming as a 100
mg dose so it becomes difficult when you are utilizing the routine practice the advantage
with new old members that is already available is 40 mg. So we do utilize new for 40 mg as
our loaders in lung cancer not a very routine phenomenon but yes when we see Pd1 is good

patient doesn't have any targetable notation we do utilize it which is out of the box and not
approved option. So overall basically this thing only cause if you go this take 50 mg you need to
buy 100 mg while the cost will be 1.6 like or 1.8 like and over appeared it will go beyond 10
like and similarly if you go standard dose and use the pap support it will again will be 10 like
or 11 like so I don't know how Kumar sir will I.
So this is the argument someone gave to me the level map also to me can you level map has now
become 7 like or something correct and you use you know 20 mg then it comes out to be a bit cheaper
but if it is used 40 it is around 35,000 rupees it comes out to be the same cost. So right now
the way Ajay used to sit with me now you know my friend her sit sit with me so they had asked
the same question to me and I tell you what I answered. So but today is that the case
tomorrow when generic comes they may come with maybe let's 20,000 rupees and 20,000 rupees
tomorrow if it is 20,000 rupees per month 100 milligram or 200 milligram while can you use
40 milligram and will that decrease the cost. So we are presuming he transiently at this moment
pap program has you know has come in a situation where today it looks that 40 milligram is not
cheaper than 200 milligram because of the pap program and I can say today will the pap program
will remain tomorrow if the generic comes. Sir is there any pap program for pemeteric
said today none then what will happen? Sir now also yes you have to pay a friend for five months
and suppose there is progression after three months when patient has already paid three
four lakhs so you if you use low dose now also it is still beneficial. I get your point. So I was
coming to many other reasons but I was saying the first reason so for me developing something
for no cost is meaningful but Ajay also has a valid reason and you know there is a good example
for it because what we develop we develop gem staphine Ajay is aware of it because we used to
be together you know some time back. So we develop gem staphine low dose versus full dose and that was
260 milligram per meter square and versus 1200 milligram per meter square but the problem was
the gem staphine by the time we developed the cost came became so low it is around 3000 or
2000 rupees then you do not save much and then the infusion infusion was six hours so not meaningful.
So it may happen tomorrow so then it does not benefit but till the cost is around in the range of
not I am talking about a lakh rupees or you know 70 000 till the cost in Indian context
I know and I will ask many people here in your practice how many people are able to take a drug
cost which is 20 000 rupees per month for year two or three years are everyone able to take it?

No I am telling good Eberatron this question was asked by Dr. Niraj Niraj said I heard Niraj
Agarwal Kappihan Eberatron Kibri cost come over here it is 6 7000 or 8000 something so as I keep come to who came to the
because we are running a protocol of 250 versus 1000 if 8000 becomes 2000 is it more meaningful
in today's time also I am asking it becomes meaningful but I concede and there your generation
has to think so this was our generation solution so your generation has to think
it's Jamsar bin Kalya Kyaa solution Hana Chita which we couldn't and is Kalya went tomorrow
immunotherapy cost becomes 3000 4000 in four five years down the line think rupee depreciates
it will be irrelevant if you give 40 or 200 then will the duration will become important
so today we give three weekly so you know you mentioned in the same protocol we are giving
Pembrozum have six weekly after four cycles in that Pembro so we thought we have not thought
you know four years down the line but your generation has to think hey after that when
it becomes relevant the patient visit to hospital become more relevant so cost for drug won't be
won't be relevant but patient will like do I come every three weeks or if I can come every three
months will that be more useful what we do in our hormonal therapy for prostate cancer
patient doesn't want to come every month they say if I can come every three months
four months so we need to think about especially for you guys you know that in future protocol
should be not for low dose I agree low dose will be relevant for few years not longer but after that
duration and how long to give that will become more patient centric
and I would add to that and low dose is still very relevant to my country Nepal in Nepal we
don't have patient support program so it's it makes a lot of difference
so I'll agree still in even corporate setting where there are significant number of patients
where we are giving still 20 mg or 40 mg new volume map I'm not able to afford the standard dose despite the PAP support and basically the PAP support again as I mentioned we need to buy a three or four or five cycles initially and pay the whole year
charges and it is not possible for everyone to pay the that amount in short duration of time
so coming to the I'll skip this one just last of last point the red gut microbiota so again
two as track was presented today and they have shown the importance of other than PDL1 and TMD
some other markers which we are doing to find the better bio marker for immunotherapy candidate
so one of the promising is the gut microbiota and these two have shown
this has the potential in the future they have everyone will adapt in clinic to alter the gut
microbiota and increase efficacy similarly there is this
metaninases where they have shown giving antibiotic between two two months before and two months
after the immunotherapy will deteriorate the outcome in terms of PFS and OS irrespective of
the kind of cancer patient is having so this is study is a good 33,000 plus

patients and they
have come to the conclusion giving antibiotic in between due while immunotherapy ongoing will
deteriorate the outcome so definitely that microbiota is the next bio marker which we need to
keep focusing on and Dr. Ather Sillser also presented when doing one research on the gut
microbiota and hopefully in future we will be able to utilize these in clinic in a more positive
way with this I'd like to thank for the give the organizer giving the opportunity and my panelists
for support thank you thank so thank you Ajahn thank you to all the panelists we now move to our
next session and Ajay will stay on stage because he'll be presenting this session which is novel
treatment options in lung cancer with focus on pembrolusumab and this is a