Hi, good morning to all of you and thank you, Organisys for this great opportunity and I'm
really glad and appreciate the Organisys for including this topic.
Yes, can you please put the power point?
Because I think it is one of the less discussed topic in any of our oncology forums or one
of the neglected topics.
So I'm glad that actually you people have included this topic.
So this about the cancer and chemotherapy related cognitive dysfunction, its contributing
factors and management.
And as a background, we all know due to the advances in the screening, early detection
and improved anti-cancer treatments, there's an increasing prevalence of cancer survey
ways.
We all are seeing more and more cancer survey ways in our practice, but it also there is an
increased concern about the long-term effects of cancer treatment.
And a common effect on cancer treatment is cancer related cognitive decline or impairment
and sometimes referred to us.
Please, please ladies and gentlemen, it is called the chemo brain or the chemo folk.
And it is actually unattended or under-cakenized thing in our practice and its impact is much
more than that we are thinking about.
So the impact of the CRCD is that it impacts the functional status of the patient, it can
affect the level of independence, it impacts the decision-making capacity of the patient
and the most important it can affect the treatment compliance, particularly in elderly
patients, they can have the pretreatment cognitive impairment itself.
And if we start the treatment, it will further worsen its cognitive function.
So it will affect the treatment compliance and it will definitely affect the quality
of life and the caregiver burden.
In our society, the most important thing is that once the patient completes treatment,
actually the family thinks that the patient is completely normal and they expect the
normal behavior or outcome from the patient.
But unfortunately, it may not be possible in several locations.
So this caregiver burden will be more and it ultimately affect the survival of the patient
also.
So if you take the prevalence of this issue, we know in the case of brain tumors, it is
pretty high, it may be due to the effect of the tumor itself or due to the effect of
the surgery, radiation or chemo.
But if you take the known CNS tumors, if you see actually statistics, it is pretty high,
that is in the case of hematological malignancies, it reaches up to 30% in the breast cancer,
it is actually around 40% and in gynecological cancer, 60% then hedonic tumors around 40%
of the callerical cancer 40 and testicular tumors 60% of the patients.

So actually it is surprising to see that actually the incidence of the prevalence in testicular
tumors is 60% of the patients, actually it is linked to the intensity of the treatment.
Actually, mainly we are using this as a stratinatal parasite in testicular tumors.
So this intensity of the treatment is also having a role and also the hormonal factor
is also having a role in the case of CCRD.
So as I mentioned, the intensity of the treatment and also the cumulative amount, it will affect
the impact on the CRCD, that is if you take a stem cell transplant in the case of lymphoma
or an alloy transplant, we usually give the conditioning before the transplant.
So the conditioning itself can cause the some amount of cognitive decline and then the way,
and after that when the patient undergoes the stem cell transplant, it can aggravate the
situation.
So it also suggests that the effect of cancer treatment on cognition may be cumulative and
if you say myelobletium regimen or a TBA in the case of an alloy transplant, it all increases
the risk of cognitive decline when compared to a reduced intensity conditioning.
So then what about the role of or the impact in the case of newer treatments like the
targeted treatment, then immunotherapy and also the newer treatment called CAR T-cell
therapy.
Actually, actually it's still warrants for this study because the data is so immature,
but we have a few data about the tyrosine kinase inhibitors in the case of renal cell
carcinomas like cuneate, it can affect the cognitive function of the patient and also
therapy using anti-vegetable agents, it can all affect the cognitive decline of the patient.
But if you see the data, if you consider immunotherapy and CAR T-cell therapy, so even though the
data is mature, actually it is not directly affecting the cognitive function of the patient.
We know I can in the case of CAR T-cell therapy, it's a different entity.
Apart from that, it is not affecting the cognitive function in the newer therapies.
So the grim reality is that the adult with the CRCD do not routinely receive attention
for cognitive concerns, especially from the oncologist.
Usually in our practice, once the patient completes treatment, we are mainly interested
about the follow-up scans, either the PET CT or the CT or ultrasound or the tumor markers.
And actually, we are not giving much importance to the cognitive dysfunction.
If the patient complains something also, we all will tell that, but what's subtic or it's all the part of the treatment.
And actually, they are not getting much attention regarding these things.
So individuals with CRCD are then forced to adapt, then despite the considerable impact
of symptoms across all their life demands.
So it's a sad state of affairs.
So if you take the older cancerous per se, the older cancer patients' data, the cognitive

disorders in older patients present, the prior to the treatment itself are often under-diagnosed
if you are not doing a CGA.
And 6 to 10% of the people above 65 years, they suffer from dementia.
And the prevalence actually approaches to 50% age in community setting in those patients
who are more than 80 years.
So the cognitive impairment associated, that is the pre-treatment cognitive impairment
is having an increased risk for progression to dementia if we start the treatment.
And the progression rates is actually around 10 to 15% per year when compared to the 1%
age in a cognitively intact patient.
And again, the 1-5th of the geriatric cancer patients can positively for cognitive disorders
in an academic setting if you are doing a proper CGA.
So coming to the pathophysiology of this problem, actually it is not completely understood.
But still the postulated, some of the factors are the genetic predisposition that is actually
the role of upper lipoprotein E, then the failure of blood-bared barrier integrity, then actually
the direct neurotoxicity due to the chemo or radiation or due to the DNA damage and then
hormonal factors, that is reduction in estrogen and testosterone may be due to the drugs or
due to the anti-indeprivation therapy or orctectomy.
Then effects of cytokines in the brain, then microvascular obstruction and infection of
the brain tissue and other psychologically based explanations include the cancer-related
fatigue, cancer-related pain and safety and depression.
So this all are the mechanisms involved actually with this problem like the neuroinflammation,
then direct neurotoxicity either due to surgery, radiation or chemo, then the hypothalamic
pituitary adenylaxis involvement and genetic polymorphisms which includes upper lipoprotein
E, then catechol omeletal transferase and brain derived this neurotrophic factor.
So it is a beautiful flow chart, it is showing the etiology outcome and the assessment.
So you can see that, you can see the cancer itself can cause cognitive dysfunction, cancer
treatment, the engentric predisposition age and comobities, then psychological, hormonal
and social factors.
All this can cause this neuroinflammation, direct neurotoxic injury and urethral dysfunction,
it all can cause this cognitive dysfunction and the patient will come with actually symptoms.
Sometimes this symptoms when we saw subtle and we have to use the patient reported cognitive
outcome measures to detect or you are to use the proper neuropsychological test to detect
that.
So what are the common symptoms that they present with?
It may be a difficulty in multitasking and sometimes trouble in concentrating, inability
to focus on tasks, then memory lapses, then difficulty following instruction,

decrease
stability to handle their personal finances, then disorganized behavior or thinking, loss
of initiative or loss of interest, then difficulty remembering the common words and recalling
names, inability to recognize familiar objects, then altered perception and difficulty in
finding the words.
So these are the most common symptoms that they encounter.
And so what are the potential contributing factors apart from this cancer and chemotherapy?
So invariably the advanced age we all know, then the frailty of the patient, then certain
medications and their side effects like if the patient is on steroids or if the patient
is on opioids for pain or if the patient is receiving any benzodiazepines or anticholinergic
it all are the confounding factors in the case of a cognitive decline.
Then hormone status and menopostural status, then emotional distress, then depression and
safety, then symptoms such as the cancer pain, cancer-related fatigue and insomnia.
And so definitely the co-mobilities, then the use of alcohol or other agents that can
alter the cognitive status of the patient, then the higher the stage of the disease,
like the stage for disease or more aggressive tumors are also associated with the increased
risk of cognitive decline.
Then so definitely increased level of CRP or other the inflammatory markers like interleukin
6, this all are the potential contributing factors.
So how to assess a cancer-related cognitive dysfunction?
It's a very, it's a very difficult question because there is no large-scale studies or
there is no standard recommendation to assess the cognitive decline in the patient with
cancer.
If you do a pediatric assessment, it provides an opportunity to identify cognitive decline.
It is often overlooked by a routine care.
So the most commonly used tools are mainly the MMSC or the MOCA or the mini-COG or the
blessed orientation memory concentration.
So this actually in our hospital actually we are mainly using MMSC but we have challenges
also.
Like this CRCD, it can co-occur with actually within the context of an age-related cognitive
decline.
So it is actually really a challenge.
So it presents two immediate challenges to precise and accurate screening.
First many of these actually cognitive screenings like the mini-COG, MOCA or MMSC
and the BOMC.
They were actually developed to screen for dementia or to assess a particular impairment
such as following a stroke.
So these syndromes are qualitatively different than the cancer-related cognitive decline.
So the commonly used screen is may not be much beneficial to assess the situation.

So in that case actually this PRO study the patient reporter outcome scales like the promise
or the four-point fact coke might prove valuable but actually it warrants further study.
So it is a flowchart actually it is showing that if the patient presents with any of the
symptoms or if the caregiver is actually telling some hints or if we can identify some
issues in our clinical examination we can start the screening.
So always remember that actually we had to roll out the confounding factors before screening
and then after screening if we identify any potential cognitive problems then actually
we can give intervention based upon that either the pharmacological or the non-pharmacological
but if it is not identified then we have to do a cross monitoring of the patient.
So this is about the role of the biomarkers in CRCD it is still investigational it also
needs further validation.
So the potential things that are described as either the biomarkers of CSF then the functional
imaging using MRI and PET scan and then the plasma markers like the interleukin-6, then
exosomes and also microarray, RNAs and then the genetic markers as I mentioned earlier
like apolepoprotein A, COMT and the BdN of but this is not a standardized recommendation
at present it is still investigational.
So coming to the management of cancer-related cognitive dysfunction so again the challenges
are it is still a poorly understood etiology then lack of constrances on best assessment
approaches either the PRIMs or other the cognitive screen is then the subtle nature of changes
in mental process related to cancer and the subjective aspects of this CRCD.
So actually the management of a CRCD we have to consider it as a continuum it includes
three important elements that is a prevention control and adjustment and actually the prevention
includes the awareness of the situation and then the education of the patient and caregivers
to pick up the symptoms early and then the close monitoring and control includes to identify
the problem by using either of these PRIMs or the cognitive screener and then interventions
either pharmacological or nova or behavior and then elevation of symptoms and adjustment
is again the follow-up of the patient by re-examination of symptoms then performance
assessment and the fine-tuning of interventions.
So coming to the non-pharmacological approaches so different approaches has been explained
or like the cognitive training CBT then the cognitive rehabilitation then the mindfulness
exercises then physical activities yoga then psychoeducation all are actually actually
recommended for as a non-pharmacological approach in CRCD and coming to the pharmacological interventions
so the NCCN clearly states that the use of non-pharmacological interventions should

be used whenever possible with the pharmacological intervention as the last line of treatment
in cancer survivors for whom the other intervention how been insufficient.
So the treatments that we can try still this all are not FDA approved actually methods
but still we can try the senes stimulants like the modafinyl or the middle fenidate or anti-dimensional drugs like the donor pestil and mametin we all know that this mametin
are being extensively used in those patients who are getting radiation and then the SSR
and also the other agents which have been tried are mainly the eartopoietin stimulating
agents like eartopoietin and also jinko palopa.
So to conclude actually the most important the message is that the long-time cognitive
impairment is an emerging health issue in cancer survivors and the awareness is most important
particularly among clinicians in order to prevent, diagnose and manage cognitive impairment
appropriately and the self-reported cognitive impairment should not be disregarded and
it should be carefully assessed and managed by that in clinician and a few words about
our work actually it's our the oncology team and this is our the geriatric oncology team
at my hospital and our hospital is the first exclusive geriatric oncology centering in
Kerala which offer the holistic geriatric oncology service and thank you for your patience.