Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting: https://reachmd.com/programs/cme/unravel-global-clinical-complexities-in-head-and-neck-cancers-identifying-approaches-to-improve-outcomes-with-manageable-toxicities/13056/

Released: 12/29/2021
Valid until: 12/29/2022
Time needed to complete: 15 minutes

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Unravel Global Clinical Complexities in Head and Neck Cancers: Identifying Approaches to Improve Outcomes with Manageable Toxicities

Announcer:
Welcome to CME on ReachMD. This activity, entitled “Unravel Global Clinical Complexities in Head and Neck Cancers: Identifying Approaches to Improve Outcomes with Manageable Toxicities” is provided by Agile.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Guigay:
So welcome to this global educational activity in squamous cell carcinoma of the head and neck. Worldwide, head and neck cancers account for approximately 900,000 cases annually, with an increasing mortality rate. With the 5-year survival rate at less than 50%, the need for both safe and effective treatments is imperative.

This is CME on ReachMD, and I am Dr. Joël Guigay.

Dr. Harrington:
And I’m Dr. Kevin Harrington.

Dr. Guigay:
Squamous cell carcinoma of the head and neck are a complex group of cancers. However, prevalence is low, the mortality rate is high, and there are certainly some unmet needs. So, Dr. Harrington, can you give us a little background information on squamous cell head and neck carcinoma and tell us what some of those unmet needs are?

Dr. Harrington:
Thanks, Joël, you’re absolutely right. With nearly 400,000 deaths every year from head and neck cancer, there really is a desperate need for us to improve treatment outcomes. And I think we can think of this in many different ways. So at the time of treatment of newly diagnosed cancer, there are many places in the world where the provision of surgery or radiation resources, in order to offer curative treatment at the very outset for patients, is not as good as we would like it to be. And unfortunately, that can lead to an increased burden of recurrent or metastatic disease. And even when we think about recurrent and metastatic disease, we know that historically, the best we’ve been able to achieve until the last few years has been a median overall survival of between 7 and 10 months. And again, that’s a fairly abysmal outcome for our patients. We’ve seen within the last decade that the use of targeted treatment options including anti-EGFR therapy such as cetuximab have moved the goalpost on that and have improved those outcomes. And more recently, we are seeing further benefits with immuno-oncology drugs. But even so, many patients receiving immuno-oncology drugs will fail to derive benefit or will ultimately progress and, again, we need to focus our thoughts on the use of combination treatments including chemotherapy and anti-EGFR-targeted drugs in order to improve outcomes for those patients. So I think there are still many challenges left in front of us.

Dr. Guigay:

We have more options now to treat these patients with, as there are many challenges in front of us, and we need to improve efficacy, and the safety of our treatment for these patients.

Balancing safety and efficacy when selecting the treatment option is an art. Dr. Harrington, how would you approach treatment-related toxicities?

Dr. Harrington:
If we think in terms of the patients for whom we're not going to use immuno-oncology drugs in the first line, those patients will receive cytotoxic chemotherapy with or without an additional anti-EGFR antibody such as cetuximab. Now, we know that those regimens are associated with quite appreciable toxicity, and that can have an impact on the patient's quality of life while at the same time hopefully delivering to them a treatment response that makes their disease better, and of course, that can improve their quality of life. So I think one of the things that we have to think about is how do we manage those toxicities around drugs such as cetuximab? And of course, with algorithms and with a lot of experience now, we've become very good at managing some of the skin toxicities, the gastrointestinal toxicities, to make this much more manageable.

I think regimens that contain 5-fluorouracil remain for many patients a problem, and that's why I think the evolution towards combinations which include docetaxel, platinum, and cetuximab, for example, the TPExtreme regimen, that really represents a very interesting direction of travel, both in terms of its deliverability, its convenience, 4 cycles instead of 6 cycles with the EXTREME regimen, and the avoidance of 5-FU-related toxicities. From my perspective, the data for TPExtreme, even though not necessarily showing an improvement in survival outcomes, represents a very interesting approach. And certainly, there is increasing interest in the use of taxane-based regimens, including, as we may discuss subsequently, in combination with immuno-oncology drugs. So I think there's a great change happening in the way we think about how to treat patients in first line and beyond.

Maybe you could give some further perspective, Joël, because I know that you have very significant experience of using regimens such as TPExtreme, and I'd be interested to hear your thoughts.

Dr. Guigay:
With the experience of the TPEx regimen using docetaxel instead of 5-FU for many years now, after the first phase 2 and now with the results of the TPExtreme trial, we have a great experience of this. Convenient for fit patients, this regimen is, in these conditions, well tolerated and, as you said, more convenient than the standard platinum 5-FU, cetuximab conventional combination. And for patients for the teams to limit 4 cycles, limit the toxicity of this regimen. And as you know, also, the doses of cisplatin are reduced inside TPEx regimen compared to the standard EXTREME regimen and best explain, also, the lower toxicity and the improvement in quality of life that we observed, especially in the real life. As you said, we use also another combination using taxane in second line or for unfit patients.

When treating patients with head and neck squamous cancer, especially in a recurrent or metastatic setting, the incorporation of current and emerging evidence into clinical practice is key. Dr. Harrington, how do you treat patients with taxanes in combination with platinums or monoclonal antibodies, and will this combination of taxanes and monoclonal antibodies have a future role in recurrent/metastatic squamous cell head and neck carcinoma?

For those, just tuning in, you're listening to, CME on ReachMD. I'm, Dr. Joël Guigay and here with me today is Dr. Kevin Harrington. We are just about to discuss the delicate balance of efficacy and tolerability of treatment options in patients with squamous cell head and neck carcinoma.

Dr. Harrington:
Well, Joël, I think this is a really important and interesting point. I think you and I can probably agree that our least favorite drug for prescribing to patients is 5-fluorouracil. It is inconvenient, I think is not the most effective drug we have at our disposal, and it's associated with quite appreciable toxicity. So I think movement away from the use of 5-FU or 5-FU-based treatment regimens is to be encouraged, and certainly I'm very keen to see research in that area.

I think we do have data, as you've so nicely discussed, around the use of TPEx, TPExtreme-type regimens where the use of a taxane instead of 5-FU gets us into a much better position. I think the taxanes, paclitaxel, docetaxel, lend themselves very nicely to combinations with carboplatin and with other drugs such as cetuximab. They lend themselves to weekly use, which is convenient for patients and for clinicians. And I think that we're going to see an increasing emphasis on these drugs. And I hope that we will see increasing numbers of clinical trials reporting in this area because certainly in my own practice in the United Kingdom, we can only prescribe these drugs based on published evidence. And so we need that evidence to justify the use of these regimens.

I think another area that is very interesting, and the use perhaps of drugs such as cetuximab, and this is in the second and greater line setting at the moment, is the use of cetuximab as a means of accentuating the activity of immuno-oncology drugs. And I'm particularly

interested, for instance, in the INTERLINK-1 protocol where the use of an immune checkpoint inhibitor now targeting NK cells trying to promote antibody-directed cellular cytotoxicity, or phagocytosis, is a really interesting way of bringing another cell, the NK cell, into the therapeutic regimen for patients with head and neck cancer. So I think those sorts of activities are particularly interesting.

I'd be interested to hear your thoughts around this. What opportunities exist in this space?

Dr. Guigay:
If we could have a chemo-free very effective combination, it would be very nice for our patients. And I agree that we had the first results of studies combining an IO agent plus cetuximab, for example, with nivolumab or avelumab, and these preliminary results seem very promising.

Another point comes from a different study, especially from the TP-EXTREME trial, looking at the sequence of taxane-based regimens such as TPEx followed by an IO agent in second line, we observed a very promising median of survival, 22 months, and that was also observed in retrospective studies conducted in many centers in France. This data opened the question of the synergistic effect between taxanes and IO agents, as we know the synergistic effect between taxane and anti-EGFR cetuximab, and also what could be the best and effective sequence in terms of combination. And is it a taxane followed by IO agent or the contrary, or in the meantime just after the first cycles of chemo?

Dr. Harrington, can you elaborate on the current treatment guidelines and how you individualize a patient's treatment plan?

Dr. Harrington:
I think that we shouldn't forget that this is what we're trained to do. Every time we select treatment for a patient, we're taking into account the individual requirements of those patients. But I think we've gone further now with some of the markers that we have. And in particular, in the first-line setting, we use routinely now the PD-L1 CPS within the tumor as a means of deciding whether or not that patient is eligible to receive immuno-oncology drugs, for instance, pembrolizumab in the first line, based around a CPS of greater than or equal to 1. But of course, we will always factor into this the general condition of the patient, the overall burden of disease, the presence of symptoms that they may have in making a decision between single-agent immunotherapy or immunotherapy in combination with cytotoxic chemotherapy.

Now, the PD-L1 test itself, as I'm sure you will agree, is an imperfect way of selecting patients for specific treatment, but it's the best that we have at the moment. I would hope that in the not-too-distant future we'll have better markers that will tell us who can and who cannot most likely benefit from individual treatment choices, cytotoxic drugs, immunotherapy, combinations of those. And of course, at all times we have to think in terms of the general condition of the patient and how we balance the efficacy of treatment with the likely toxicity and what the overall output of that treatment will be both in terms of disease control and quality of life. So it remains a complex equation, something that we juggle on a daily basis in our practice. And again, Joël, I'll be interested to hear your thoughts because I'm sure you have similar but maybe slightly different approaches to this.

Dr. Guigay:
We need to have a clear and careful evaluation of our patients before making a decision, especially in first line. We have many clinical factors that are very important to make this decision of the best treatment to propose to our patients.

Can you share your one take-home message with our audience?

Dr. Harrington:
Joël, I think the single message I'd like to leave the audience with, in the midst of this IO era, we mustn't forget that cytotoxic chemotherapy and anti-EGFR therapies have a significant place to play in the treatment of our patients. And again, I would emphasize the fact that where we need a rapid response, that we should consider the possibility of using taxane, platin, and cetuximab-based regimens, potentially with the avoidance 5-fluorouracil, as a means of optimizing care for our patients.

Dr. Guigay:
Unfortunately that's all the time we have today. I want to thank our audience for listening in and thank you, Dr. Harrington, for joining me and for sharing all of your valuable insights.

Dr. Harrington:
Joël, as always, it was a pleasure to speak with you, and I look forward to seeing you in the not-too-distant future.

Announcer:
You have been listening to CME on ReachMD. This activity is provided by Agile.

To receive your free CME credit, or to download this activity, go to ReachMD.com/Agile. Thank you for listening.