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/what-is-the-current-standard-for-first-line-treatment-of-metastatic-her2-negative-ggej-cancers/18025/

Released: 02/05/2024
Valid until: 02/05/2025
Time needed to complete: 42m

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

What Is the Current Standard for First-Line Treatment of Metastatic HER2-Negative G/GEJ Cancers?

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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

Dr. Janjigian:
Hello, my name is Dr. Yelena Janjigian. I'm a Medical Oncologist at Memorial Sloan Kettering Cancer Center focused in upper GI malignancies. And it's a pleasure to be able to update you on the current standard for first-line treatment of metastatic HER2-negative gastric and gastroesophageal adenocarcinoma.

So, by way of background, the last 2 years have been quite transformative in our disease. And the current ASCO and NCCN guidelines really incorporate use of anti-PD1 therapy in first-line cytotoxic chemotherapy combination. So, the typical backbone is fluoropyrimidine and platinum chemotherapy, or FOLFOX, or CAPOX, and then we add anti-PD1 therapy to it. And we have approvals both for nivolumab and pembrolizumab in first-line setting; both, you know, pembrolizumab is approved both in HER2-positive and HER2-negative disease.

So, a lot of discussion comes into the cutoff for treatment of these first-line patients. As you recall, the FDA approved those agents irrespective of PD-L1 status. And also, by way of background, we know that the majority of our patients, more than close to 80%, overexpress PD-L1 to some degree in their tumor. So, then the question is, where do you draw that cutoff? And that's where all the guidelines, the expert guidelines from ASCO and NCCN come in. For example, currently, most guidelines restrict use of these agents or recommends considering restricting use of these agents for patients with higher PD-L1 overexpression, with PD-L1 at least CPS 1 or greater. And these are the guidelines that are summarized here.

So, what led to this data? Well, the first study was CheckMate 649 data that randomized patients across three arms and were looking at FOLFOX/nivo versus FOLFOX arm. This was a global study that enrolled patients irrespective of PD-L1 status, and then patients were stratified by PD-L1 status with a primary endpoint of treatment in PD-L1 CPS 5 or greater in the outcomes both of OS and progression-free survival. So, it's nice for the first time to be able to report, you know, in clinical trials, 3- and 4- and 5-year follow-up data.

So, this is 36 months, of 3-year follow-up data. And as you can see here, the hazard ratio for PD-L1 CPS 5 or greater population, biomarker selection helps identify patients who do better on these regimens, hazard ratio of 0.7. So, the curves separate early, and sustained separation of the curve was 13% of patients versus 8% alive at 36 months. And the shape of the curve is very similar for all randomized patients because that 60% of patients are CPS 5 or greater, so the shape is similar, but the hazard ratio is 0.79, suggests that perhaps selecting patients in some way may be helpful after all.

The overall survival is also improved. The median delta is improved 14.4 versus 11.1 months in CPS 5 or greater and 13.7 versus 11.6 months. But again, what we really get excited about is these long-term survivors, 17% in unselected patient population are surviving at 36 months, which is the best standard. This is the first trial that showed that we can cross the median overall survival threshold of 1 year.

© 2024 ReachMD

Historically, phase 3 studies in this disease showed only 9 months median survival and so forth.

KEYNOTE-859 recently read out, and this was a similar study looking at pembrolizumab, also in unselected population, also global study, large study looking at with again oxaliplatin backbone, which is what really should be used in patients. They tolerate it much better than cisplatin. And looking overall in CPS 1 or greater and CPS 10 or greater, almost identical sort of data and trend. And once again, we know that higher PD-L1 overexpression heralds better outcome but also in low PD-L1 overexpression, even in CPS 1 patients, maybe there's some benefit, hazard ratio 0.74. For CPS 10 or greater, the pembro/chemotherapy resulted in median OS of 15.7 months. I mean, that's really great data. But even in allcomers, the median OS is the 12.9, which is a for the first time able to cross that 1-year mark, is very satisfying.

The secondary endpoints of PFS, overall response rate, and disease control rate are all improved with the addition of anti-PD1 to chemotherapy highlighting the importance of use. And the delta here for PD-L1 CPS 1 or greater, overall response rate improvement of approximately 10%, is really clinically meaningful.

So, in summary, it's important to understand the use of anti-PD1 therapy is standard practice in first-line setting in HER2-negative esophageal and gastric adenocarcinoma, in combination with chemotherapy. Based on the results of KEYNOTE-859 data, pembrolizumab with chemotherapy is approved by the FDA on November 16th for metastatic HER2-negative disease irregardless of PD-L1 expression.

Announcer:
You have been listening to CME on ReachMD. This activity is jointly provided by Global Learning Collaborative (GLC) and TotalCME, LLC. and is part of our MinuteCE curriculum.

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

© 2024 ReachMD