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On the Frontline: Empowering IO Therapies for Patients with HER2-Negative G/GEJC

Announcer:
You're listening to *Project Oncology* on ReachMD. This program, titled "On the Frontline: Empowering IO Therapies for Patients with HER2-Negative G/GEJC," is sponsored by BeOne Medicines. Dr. Jun Gong received compensation from BeOne for their participation in this video. And now, here's your host, Dr. Charles Turck.

Dr. Turck:
Welcome to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and joining me today to discuss first-line IO therapies for patients with HER2 negative gastric or gastroesophageal junction cancer, otherwise known as G/GEJC, is Dr. Jun Gong. He's an Associate Professor and a GI medical oncologist at Cedars-Sinai Cancer Center in Los Angeles. Dr. Gong, thanks for being here today.

Dr. Gong:
Thank you for having me here.

Dr. Turck:
So, Dr. Gong, let's jump right in. What unmet needs are we currently facing when it comes to first-line treatment of G/GEJC?

Dr. Gong:
Well, gastric cancer is the fifth most common cancer worldwide and the fifth leading cause of cancer death.[1] It's an aggressive cancer, and patients are often diagnosed at advanced stages of the disease. For patients who are diagnosed with metastatic disease, the five-year overall survival rate is roughly seven percent.[2] This underscores the urgent need for additional treatment options for these patients.

Dr. Turck:
And with that context in mind, I'd like to focus on patients who are HER2 negative, a group that comprises roughly 80 percent of those with gastric cancer.[3] Would you discuss the current immunotherapy treatments available for patients with unresectable or metastatic HER2 negative G/GEJC?

Dr. Gong:
Fortunately, there's been quite a bit of advancement in gastric cancer treatment, which gives patients more options. Today we will focus on immunotherapy treatment for patients with unresectable or metastatic disease.

For patients with unresectable or metastatic disease who are PD-L1 positive—defined by PD-L1 greater than or equal to one—the standard of care is anti-PD-1 plus chemotherapy. Chemotherapy regimen typically consists of a platinum plus a fluoropyrimidine, which is reflected in the NCCN Guideline.[4]

Dr. Turck:
Now, you mentioned that there are some emerging treatment options. Would you tell us about the most recently approved immunotherapy for patients with unresectable or metastatic G/GEJC?

Dr. Gong:
I'd be happy to. The latest FDA approval for these patients is tislelizumab in combination with platinum and fluoropyridine-based chemotherapy.

Tislelizumab is a humanized anti-PD-1 monoclonal antibody engineered to minimize Fc-gamma receptor binding on macrophages, thereby reducing antibody-dependent phagocytosis of T cells.[5]

It exhibits several preclinical differentiating characteristics compared to other PD-1 inhibitors. It has high binding affinity to PD-1, which has a larger coverage of the PD-1/PD-L1 binding pocket than nivolumab and pembrolizumab. Preclinical data showed tislelizumab completely blocked the binding of PD-1 to PD-L1, while nivolumab and pembrolizumab showed partial inhibition of this binding.[6]

The high binding affinity leads to slower dissociation from PD-1 receptor. This potentially allows more time for T cells to proliferate and tumor kill. And compared to nivolumab and pembrolizumab, the dissociation rate for tislelizumab was 30- to 80-fold slower, respectively.[6]

Dr. Turck:
Thanks for walking us through those features, Dr. Gong. And shifting gears now, would you tell us about the trial design that resulted in FDA approval of tislelizumab for first-line treatment of G/GEJC?

Dr. Gong:
Absolutely, Dr. Turck. The study was called RATIONALE-305, and it was a randomized, double blind, global, phase 3 clinical trial. Patients with histologically confirmed, locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma were recruited. They were required to be HER2 negative, have an ECOG performance status of zero or one, and have at least one measurable or non-measurable lesion. They also could not have had previous treatment with anti-PD-1/PD-L1 therapies or other checkpoint inhibitors and had to have received no prior systemic therapy for advanced or metastatic disease.

The study was stratified by region, PD-L1 expression (with 5 percent as the cutoff), peritoneal metastases status, and investigator's choice of chemotherapy, including capecitabine and oxaliplatin or 5-fluorouracil and cisplatin.[7]

The experimental arm was tislelizumab 200 mg IV every three weeks plus chemotherapy, versus the control arm, which was placebo plus chemotherapy. Treatment continued until unacceptable toxicity or disease progression.[7]

997 patients were enrolled in this study with a 1:1 randomization. The primary endpoint was overall survival for patients with PD-L1 greater than or equal to five percent and in the intent to treat population. The key secondary endpoints included additional efficacy outcomes, such as PFS and ORR, as well as safety.[7]

Dr. Turck:
And with that in mind, how did tislelizumab perform in RATIONALE-305?

Dr. Gong:
Great question, Dr. Turck. For the purposes of today's discussion, I'm going to focus on the results that were published for patients with PD-L1 greater than or equal to one percent, which aligned with the FDA approval for this indication.

But before I dive into the results, I'd like to briefly go over the demographic characteristics in the groups receiving tislelizumab plus chemotherapy and those receiving placebo plus chemotherapy, which were quite consistent. The median age group was 61 years old, with roughly 70 percent of patients being male. About two thirds of the patients had an ECOG performance status of one, almost every patient had metastatic disease upon study entry, and most patients had gastric cancer at the primary location of the tumor. In terms of distant metastasis, roughly 40 percent of patients had liver metastasis and about 44 percent of patients had peritoneal metastasis.[1]

About 90 percent of patients had MSI-stable or mismatch repair proficient disease. 20 percent of patients had received previous adjuvant or neoadjuvant treatment, and most patients received CAPOX as the chemotherapy of choice. As for drug exposure, the median duration of treatment was 5.9 months for the tislelizumab arm and 5.7 months for the placebo arm.[1]

Now, in terms of efficacy, tislelizumab plus chemotherapy resulted in a clinically meaningful improvement in overall survival as compared to placebo plus chemotherapy. The median overall survival was 15.0 months versus 12.8 months, with a hazard ratio of 0.78. It was a 2.2-month difference in OS benefit improvement with tislelizumab plus chemotherapy combination. At the three-year long-term follow-up, OS improvement was maintained with tislelizumab plus chemotherapy, and the tail end of the curves remained separated. Lastly, the estimated three-year OS rates were 21 percent versus 13 percent, respectively.[1]

Dr. Turck:
For those just tuning in, you're listening to *Project Oncology* on ReachMD.

I'm Dr. Charles Turck, and today I'm speaking with Dr. Jun Gong about the latest immunotherapy for patients with first-line HER2 negative gastric or gastroesophageal junction cancer.

So, Dr. Gong, let's continue our discussion of RATIONALE-305. What did the study find regarding prespecified patient subgroups?

Dr. Gong:
In the predefined subgroup analyses for overall survival, a consistent improvement in OS was observed across key subgroups, favoring the tislelizumab plus chemotherapy combination.[1]

The subgroups worth highlighting are the primary tumor location—either stomach or gastro-esophageal junction— patients with or without liver metastasis, and patients with or without peritoneal metastasis.

Dr. Turck, you may recall one of the stratification factors in this study was the presence or absence of peritoneal metastasis, which is unique for studies in first-line G/GEJC. We know that patients with peritoneal metastasis have a poor prognosis,[8] so it's good to see it being incorporated as a stratification factor to ensure balance of patients in each arm. The subgroup analysis examining the patients with peritoneal mets showed a hazard ratio of 0.81, indicating patients with peritoneal metastasis had 19 percent reduction in the risk of death when they received tislelizumab plus chemotherapy combination as compared with placebo plus chemotherapy.[1]

Dr. Turck:
I see. And when it comes to safety, what did the study find on the tislelizumab plus chemotherapy combination?

Dr. Gong:
The safety profile of tislelizumab in this study was found to be generally manageable. Treatment-related adverse events were

reported in 97 percent versus 96 percent of patients in both the tislelizumab plus chemotherapy arm and the placebo plus chemotherapy arm. 54 percent versus 50 percent of patients experienced grade 3 or higher treatment-related adverse events respectively, and 23 percent versus 15 percent experienced serious treatment-related adverse events respectively.[7]

A total of 31 percent of patients in the tislelizumab plus chemotherapy arm experienced immune-mediated adverse events, with most of them being grade 1 and 2. For treatment-related adverse events that led to treatment discontinuation, there were 16 percent in the tislelizumab plus chemotherapy arm and 8 percent in the placebo plus chemotherapy arm. Six patients in the tislelizumab plus chemotherapy arm had treatment-related adverse events that led to death, including four patients with unspecified death, one due to colitis, and one due to sepsis. In the placebo plus chemotherapy arm, it was two patients.[7]

Overall, the most common treatment-related adverse events in both treatment arms were consistent with the known safety profile of these therapies.[7]

The most common grade 3 or grade 4 treatment related adverse events were decreased neutrophil count, decreased platelet count, neutropenia, and anemia. Finally, the incidence was comparable between the two arms.[7]

Dr. Turck:
Thank you for this insightful interview of the RATIONALE-305 data, Dr. Gong. Before we come to the end of our program, what are the main takeaways you want the audience to remember from today's discussion?

Dr. Gong:
Well, Dr. Turck, there are several key points that I want to call attention to.

Firstly, tislelizumab is a humanized anti-PD-1 monoclonal antibody, and it exhibits several preclinical differentiating characteristics compared to other PD-1 inhibitors. Tislelizumab has a high binding affinity, slower dissociation rate, and silent Fc region.[6]

Next, in the global RATIONALE-305 study, tislelizumab plus chemotherapy demonstrated a median overall survival of 15.0 months, an improvement of 2.2 months in OS versus placebo plus chemotherapy for patients with PD-L1 greater than or equal to one percent, with a hazard ratio of 0.78. Notably, in a subgroup analysis for patients with peritoneal metastasis, tislelizumab plus chemotherapy also showed favorable overall survival compared to placebo plus chemotherapy. This was the only first-line GC study that used peritoneal metastases as a stratification factor for randomization.[1]

The safety profile was also generally manageable, and there were no new safety signals detected. The toxicity of chemotherapy did not appear to worsen with the addition of tislelizumab.[7]

Finally, based on these results, tislelizumab plus chemotherapy is approved for first-line treatment of unresectable or metastatic G/GEJC with tumors that express PD-L1 greater than or equal to one, and is also listed as a preferred treatment option in the NCCN Guideline.[4] The dosing of tislelizumab in RATIONALE 305 was 200 mg IV every three weeks. Tislelizumab is approved for every two weeks, every three weeks, every four weeks, and every six weeks by the FDA. These different dosing schedules may help offer additional treatment flexibility and convenience.[9]

Dr. Turck:
That's a great way to round out our discussion, and I want to thank my guest, Dr. Jun Gong, for helping us better understand an additional first-line treatment option for patients with HER2 negative gastric or gastroesophageal junction cancer.

Dr. Gong, it was great speaking with you today.

Dr. Gong:
Thank you, Dr. Turck for having me, and it was great talking about this new standard option in these patients.

Dr. Turck:
For ReachMD, I'm Dr. Charles Turck. Before we close, let's take a moment to review some important safety information.

Announcer:

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Severe and Fatal Immune-Mediated Adverse Reactions

TEVIMBRA is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death receptor-1 (PD-1) or PD-ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune mediated adverse reactions.

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue. Immune-mediated adverse reactions can occur at any time after starting treatment with a PD-1/PDL1 blocking antibody. While immune-mediated adverse reactions usually manifest during treatment with PD-1/PD-L1 blocking antibodies, immune-mediated adverse reactions can also manifest after discontinuation of PD-1/PD-L1 blocking antibodies. Important immune-mediated adverse reactions listed here may not include all possible severe and fatal immune-mediated reactions.

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1 blocking antibodies. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

Withhold or permanently discontinue TEVIMBRA depending on severity. In general, if TEVIMBRA requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroids.

Immune-Mediated Pneumonitis
TEVIMBRA can cause immune-mediated pneumonitis, which can be fatal. In patients treated with other PD-1/PD-L1 blocking antibodies, the incidence of pneumonitis is higher in patients who have received prior thoracic radiation.

Immune-mediated pneumonitis occurred in 4.7% (113/2390) of patients receiving TEVIMBRA, including fatal (0.1%), Grade 4 (0.3%), Grade 3 (1.4%), and Grade 2 (1.9%) adverse reactions. Pneumonitis led to permanent discontinuation of TEVIMBRA in 44 (1.8%) patients and withholding of TEVIMBRA in 40 (1.7%) patients.

Eighty-one (71.7%) of the 113 patients received systemic corticosteroids. Seventy-four (65.5%) of the 113 patients received high-dose systemic corticosteroids. Immune-mediated pneumonitis resolved in 48.7% of the 113 patients. Of the 40 patients in whom TEVIMBRA was withheld for pneumonitis, 26 (65%) reinitiated TEVIMBRA after symptom improvement; of these, 5 (19%) patients had recurrence of pneumonitis.

Immune-Mediated Colitis
TEVIMBRA can cause immune-mediated colitis, which can be fatal. Cytomegalovirus infection/reactivation has been reported in patients with corticosteroid-refractory immunemediated colitis treated with PD-1/PD-L1 blocking antibodies. In cases of corticosteroidrefractory colitis, consider repeating infectious workup to exclude alternative etiologies.

Immune-mediated colitis occurred in 0.8% (19/2390) of patients receiving TEVIMBRA, including Grade 3 (0.3%) and Grade 2 (0.4%) adverse reactions. Colitis led to permanent discontinuation of TEVIMBRA in 5 (0.2%) patients and withholding of TEVIMBRA in 10

(0.4%) patients. Seventeen (89.5%) of the 19 patients received systemic corticosteroids. Twelve (63.2%) of the 19 patients received high-dose systemic corticosteroids. Two (10.5%) of the 19 patients received immunosuppressive treatment. Immune-mediated colitis resolved in 89.5% of the 19 patients. Of the 10 patients in whom TEVIMBRA was withheld for colitis, 9 (90%) reinitiated TEVIMBRA after symptom improvement; of these, 2 (22%) patients had recurrence of colitis.

Immune-Mediated Hepatitis

TEVIMBRA can cause immune-mediated hepatitis, which can be fatal. Immune-mediated hepatitis occurred in 1.3% (30/2390) of patients receiving TEVIMBRA, including Grade 4 (0.3%), Grade 3 (0.6%), and Grade 2 (0.3%) adverse reactions. Immunemediated hepatitis led to permanent discontinuation in 6 (0.3%) patients and withholding of TEVIMBRA in 19 (0.8%) patients. Twenty-five (83.3%) of the 30 patients received systemic corticosteroids. Twenty-four (80%) of the 30 patients received high-dose systemic corticosteroids. Two (6.7%) of the 30 patients received immunosuppressive treatment. Immunemediated hepatitis resolved in 66.7% of the 30 patients. Of the 19 patients in whom TEVIMBRA was withheld for hepatitis, 7 (37%) reinitiated TEVIMBRA after symptom improvement; of these, 1 (14%) patient had recurrence of hepatitis.

Immune-Mediated Endocrinopathies

Adrenal Insufficiency

TEVIMBRA can cause immune-mediated adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold TEVIMBRA depending on severity.

Immune-mediated adrenal insufficiency occurred in 0.5% (12/2390) of patients receiving TEVIMBRA, including Grade 4 (0.04%), Grade 3 (0.2%), and Grade 2 (0.3%) adverse reactions. Adrenal insufficiency did not lead to permanent discontinuation of TEVIMBRA. TEVIMBRA was withheld in 10 (0.4%) patients. All 12 patients received systemic corticosteroids. Three (25%) of the 12 patients received high-dose systemic corticosteroids. Adrenal insufficiency resolved in 25% of the 12 patients. Of the 10 patients in whom TEVIMBRA was withheld for adrenal insufficiency, 8 (80%) reinitiated TEVIMBRA after symptom improvement; of these, none of the patients had recurrence of adrenal insufficiency.

Hypophysitis

TEVIMBRA can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as clinically indicated. Withhold or permanently discontinue TEVIMBRA depending on severity.

Hypophysitis/hypopituitarism occurred in 0.3% (6/2390) of patients receiving TEVIMBRA; all were Grade 2 (0.3%). Hypophysitis did not lead to permanent discontinuation of TEVIMBRA. TEVIMBRA was withheld in 1 (0.04%) patient. Five (83.3%) of the 6 patients received systemic corticosteroids. One (17%) of the 6 patients received high-dose systemic corticosteroids. Hypophysitis/hypopituitarism resolved in 17% of the 6 patients. For the 1 patient where TEVIMBRA was withheld for hypophysitis/hypopituitarism, there was no recurrence of hypophysitis/hypopituitarism.

Thyroid Disorders

TEVIMBRA can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement for hypothyroidism or institute medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue TEVIMBRA depending on severity.

Thyroiditis: Immune-mediated thyroiditis occurred in 1% (25/2390) of patients receiving TEVIMBRA, including Grade 2 (0.5%) adverse reactions. Thyroiditis did not lead to permanent discontinuation of TEVIMBRA. TEVIMBRA was withheld in 5 (0.2%) patients. Two (8%) of the 25 patients received systemic corticosteroids. Thyroiditis resolved in 36% of the 25 patients. All 5 patients in whom TEVIMBRA was withheld for thyroiditis reinitiated TEVIMBRA after symptom improvement; of these, 1 (20%) patient had recurrence of thyroiditis.

Hyperthyroidism: Immune-mediated hyperthyroidism occurred in 4.9% (118/2390) of patients receiving TEVIMBRA, including Grade 3 (0.04%) and Grade 2 (0.9%) adverse reactions. Hyperthyroidism led to the permanent discontinuation of TEVIMBRA in 1 (0.04%) patient and withholding of TEVIMBRA in 7 (0.3%) patients. Three (2.5%) of the 118 patients received systemic corticosteroids. Hyperthyroidism resolved in 76.3% of the 118 patients. Of the 7 patients in whom TEVIMBRA was withheld for hyperthyroidism, 5 (71.4%) reinitiated TEVIMBRA after symptom improvement; of these, none of the patients had recurrence of hyperthyroidism.

Hypothyroidism: Immune-mediated hypothyroidism occurred in 12.5% (299/2390) of patients receiving TEVIMBRA, including Grade 4 (0.04%), Grade 3 (0.04%), and Grade 2 (6.7%) adverse reactions. TEVIMBRA was permanently discontinued in 2 (0.1%) patients and treatment was withheld in 12 (0.5%) patients. Two (0.7%) of the 299 patients received systemic corticosteroids. One hundred ninety-five

patients received hormone replacement therapy. Hypothyroidism resolved in 34.4% of the 299 patients. The majority (83.6%) of patients with hypothyroidism required long-term thyroid hormone replacement. Of the 12 patients in whom TEVIMBRA was withheld for hypothyroidism, 11 (91.7%) reinitiated TEVIMBRA after symptom improvement; of these, 2 (18.2%) patients had recurrence of hypothyroidism.

Type 1 Diabetes Mellitus, which can present with Diabetic Ketoacidosis

Diabetes mellitus has been reported with PD-1/PD-L1 blocking antibodies. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold or permanently discontinue TEVIMBRA depending on severity.

Diabetes mellitus occurred in 0.7% (16/2390) of patients receiving TEVIMBRA, including Grade 4 (0.1%), Grade 3 (0.3%), and Grade 2 (0.3%) adverse reactions. TEVIMBRA was permanently discontinued in 4 (0.2%) patients, and TEVIMBRA treatment was withheld in 4 (0.2%) patients. Fourteen of the 16 patients received insulin therapy for diabetes mellitus. Diabetes mellitus resolved in 12.5% of the 16 patients. Of the 4 patients in whom TEVIMBRA was withheld for diabetes mellitus, 1 (25%) patient reinitiated TEVIMBRA after symptom improvement.

Immune-Mediated Nephritis with Renal Dysfunction
TEVIMBRA can cause immune-mediated nephritis, which can be fatal.

Immune-mediated nephritis with renal dysfunction occurred in 0.2% (5/2390) of patients receiving TEVIMBRA, including Grade 3 (0.04%) and Grade 2 (0.1%) adverse reactions. TEVIMBRA was permanently discontinued in 1 (0.04%) patient and treatment was withheld in 3 (0.1%) patients. Three (60%) out of 5 patients received systemic corticosteroids. Three (60%) of the 5 patients received high-dose systemic corticosteroids. Nephritis with renal dysfunction resolved in 40% of the 5 patients. Of the 3 patients in whom TEVIMBRA was withheld for nephritis, 2 (66.7%) reinitiated TEVIMBRA after symptom improvement and no patients had recurrence of nephritis.

Immune-Mediated Dermatologic Adverse Reactions
TEVIMBRA can cause immune-mediated rash or dermatitis. Cases of severe cutaneous adverse reactions (SCARs), including exfoliative dermatitis, Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN), have been reported, some with fatal outcome. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold or permanently discontinue TEVIMBRA depending on severity.

Immune-mediated dermatologic adverse reactions occurred in 13% (311/2390) of patients receiving TEVIMBRA, including Grade 4 (0.1%), Grade 3 (1.1%), and Grade 2 (3.4%) adverse reactions. Stevens-Johnson syndrome occurred in 1 (0.04%) patient. Dermatologic adverse reactions led to permanent discontinuation of TEVIMBRA in 3 (0.1%) patients and withholding of TEVIMBRA in 30 (1.3%) patients. Forty-four (14.1%) of the 311 patients received systemic corticosteroids. Nineteen (6.1%) of the 311 patients received high-dose systemic corticosteroids. Immune-mediated skin reactions resolved in 66.9% of the 311 patients. Of the 30 patients in whom TEVIMBRA was withheld for dermatologic adverse reactions, 26 (86.7%) reinitiated TEVIMBRA after symptom improvement; of these, 3 (12%) patients had recurrence of immune mediated dermatologic adverse reactions.

Other Immune-Mediated Adverse Reactions

The following clinically significant immune-mediated adverse reactions occurred at an incidence of less than 1% in 2390 patients who received TEVIMBRA or were reported with the use of other PD-1/PD-L1 blocking antibodies. Severe or fatal cases have been reported for some of these adverse reactions.

Cardiac/Vascular: Myocarditis, pericarditis, vasculitis.

Nervous System: Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barre syndrome, nerve paresis, autoimmune neuropathy.

Ocular: Uveitis, iritis, and other ocular inflammatory toxicities. Some cases can be associated with retinal detachment. Various grades of visual impairment, including blindness, can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a VogtKoyanagi-Harada–like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss.

Gastrointestinal: Pancreatitis including increases in serum amylase and lipase levels, gastritis, duodenitis, stomatitis.

Musculoskeletal and Connective Tissue: Myositis/polymyositis/dermatomyositis, rhabdomyolysis and associated sequelae including renal failure, arthritis, polymyalgia rheumatica.

Endocrine: Hypoparathyroidism.

Other (Hematologic/Immune): Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenia, solid organ transplant rejection, other transplant (including corneal graft) rejection.

This program was sponsored by BeOne Medicines. If you missed any part of this discussion, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge.

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