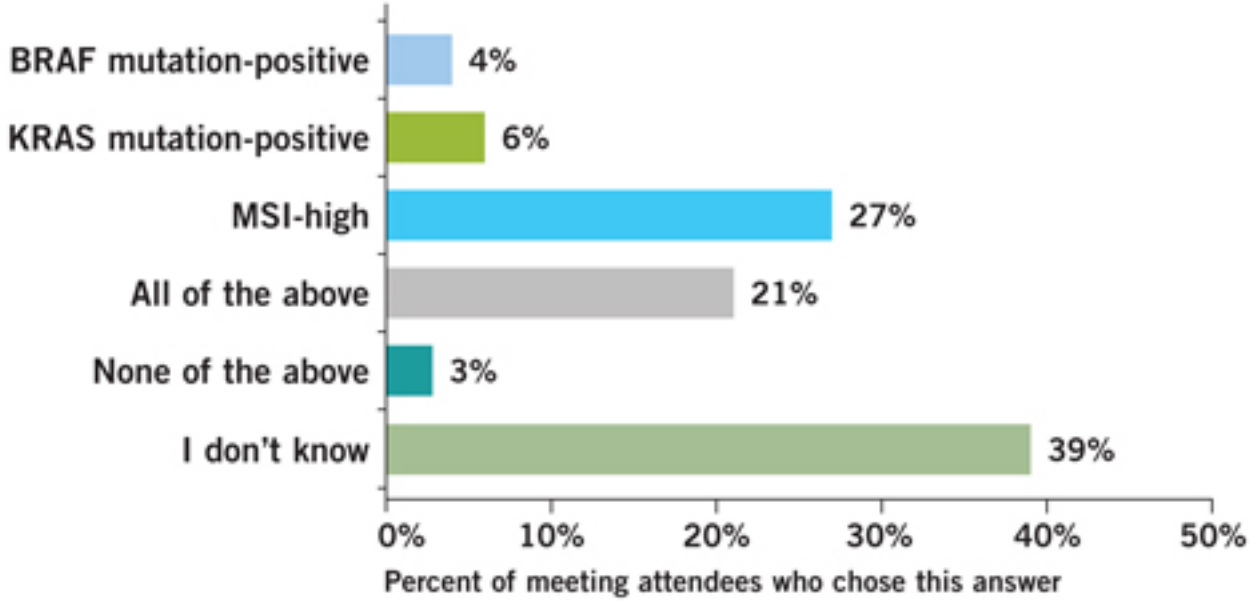
Year in Review

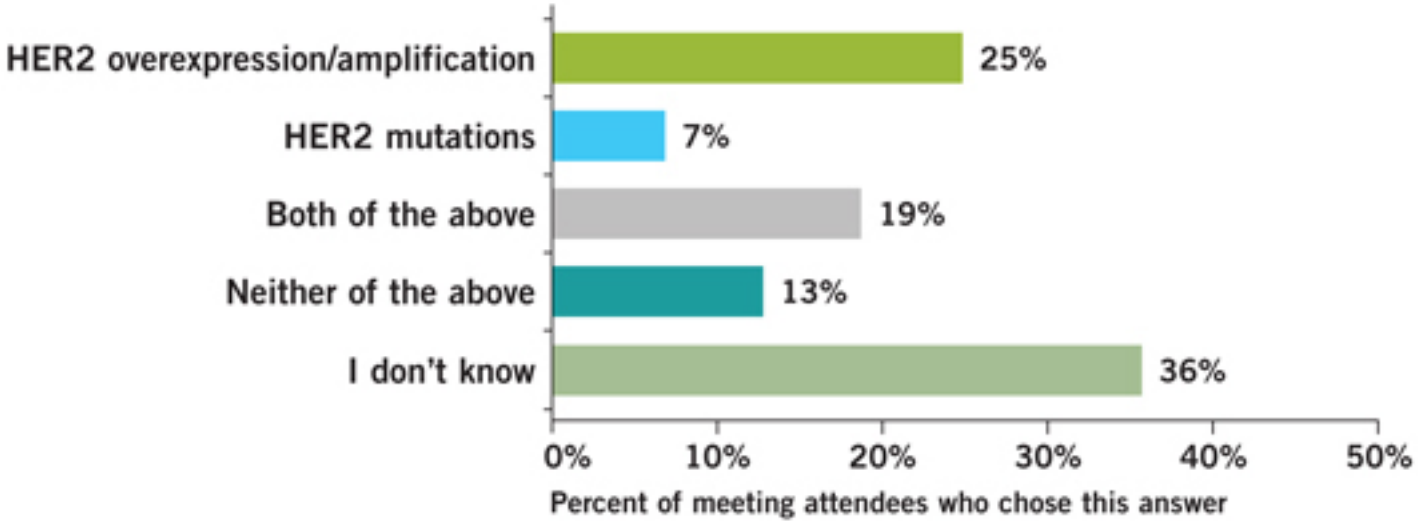
Proceedings from a Multitumor CME Symposium Focused on the Application of Emerging Research Information to the Care of Patients with Common Cancers

Emerging Data on the Treatment of Metastatic Colorectal Cancer — Axel Grothey, MD

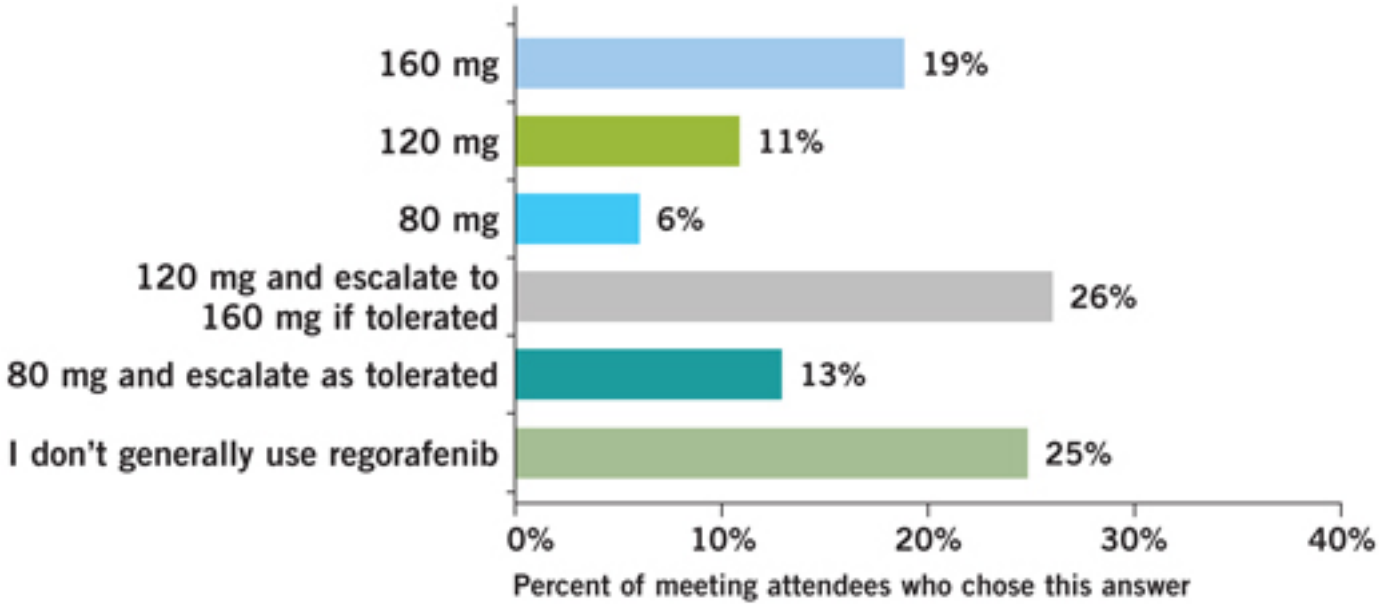
Which of the following subsets of patients with metastatic colorectal cancer (mCRC) have been shown to experience clinical benefit from an anti-PD-1 antibody?



Patients with mCRC and which of the following tumor alterations have been shown to derive benefit from anti-HER2 therapy?



In general, for a younger otherwise healthy patient with mCRC, which starting dose of regorafenib would you use (daily for 21 days of every 28-day cycle)?



DR LOVE: Whenever we ask this, Axel, we get a whole spectrum of answers, and that's what we're seeing here today. Simple question: How do you start out your dose of regorafenib? Practically speaking, I'm curious what each of you do. Axel, how do you start out the dosage?

DR GROTHEY: I start at 80 mg for 1 week and then go up 120 to 160 mg. It's a 3-week cycle, 3 weeks on, 1 week off. I really ease things in because side effects come early. I really try to buffer the first 1 or 2 weeks by using a lower dose and monitoring patients on a weekly basis. But I'm very cautious.

DR LOVE: Johanna?

DR BENDELL: I've always said 80, but now I think it depends on the patient. For this particular question, I answered 120 and then escalate because with the younger, healthy patients where I know that they're going to be good historians and reliable in getting back to me if they have side effects, I start at 120.

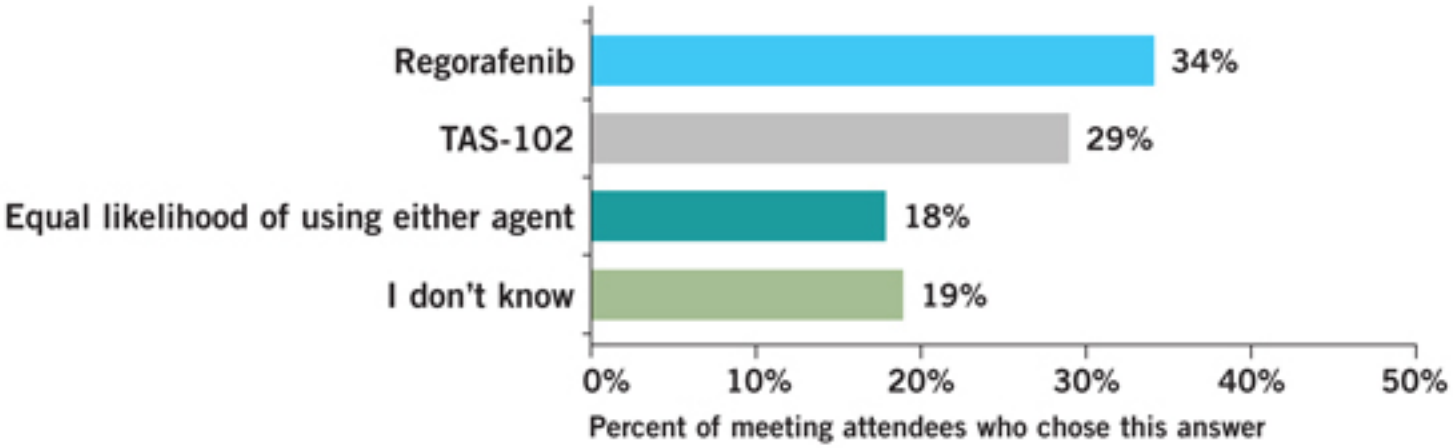
DR LOVE: Axel, we've talked about so many new agents coming in that also affect the support staff within the oncology office and the structure of how these patients are followed. What exactly do you do with your patients starting on regorafenib? When do they come back? When do you call them? When do they call you?

DR GROTHEY: We have contact with them at least on a weekly basis for the first 2 cycles. Some patients that come to Rochester come from far away, so they might not physically come back. We have a nurse call them and talk about how things are. We need liver enzymes after 2 weeks. Some of these patients come from 7 hours away. They cannot come in for just liver enzyme or clinical visit. We stay in touch with them by phone or physically on a weekly basis.

DR LOVE: Axel, maybe you can talk for a second about the typical clinical syndrome that you see. Is it worse in the cold?

DR GROTHEY: It's not worse in the cold, as, actually, that's good because there are papers on the use of oxaliplatin above the polar circle. And that sounds like Minnesota. We can use oxaliplatin in Minnesota. Regorafenib is independent of cold, but what happens when patients develop side effects is, mainly, it affects their feet more than their hands. It affects the feet in terms of, sometimes, blisters, which makes the patients unable to walk within the first 2 weeks. When I talk to patients up front, I tell them, "Remove calluses. Wear comfortable shoes. Get a pedicure, not to paint your toenails, but to really get your skin smoothened up," because that is the main important point that patients need to know before they start regorafenib.

In general, which agent would you most likely use first for a patient who has received multiple prior treatments for mCRC?



DR LOVE: Johanna, we now have an interesting choice in clinical day-to-day management that we didn't have a couple of weeks ago. We've been talking about TAS-102 now for about a year, and it's here. Now we have two agents approved in the later-line setting, both regorafenib and TAS-102. You can see the audience is a little bit not clear about what's going to be first. How are you going to be thinking this through?

DR BENDELL: It's interesting. When you look at both studies from a general perspective and the benefit that was seen in terms of survival from each agent, the overall numbers suggest about the same benefit for each agent. Then the question becomes: What's the side-effect profile? And I think that that's going to be a big player in determining which agent you choose first.

With TAS-102, at least in our hands — I know it has a long list of potential side effects, but really what we saw when we used it was a decrease in blood counts, so white blood cell count, platelets and red cell count. That was the biggest side effect that we really saw in people. I think that's a lot different than what we see with regorafenib. I think that as people start to use these agents a little bit more, there may be a little bit more of a trend toward the TAS-102, just because we can handle blood counts a little easier sometimes than the fatigue and hand-foot syndrome that we see with the regorafenib.

DR LOVE: Axel, what's your take on this in terms of sequence?

DR GROTHEY: My mantra is to make all drugs available to all patients. My concern is, regorafenib is a more difficult drug to use. We should not use regorafenib in PS 2 patients. If you have a more heavily pretreated patient they might not benefit from regorafenib at all. In a healthy, good performance status patient, I normally use regorafenib before TAS-102 because I want to make sure that patients receive all agents.

In a patient who's on the fence in terms of performance status, et cetera, I think regorafenib might not even be a choice. TAS-102 is easier to use in these patients. I think the patient pool that can tolerate TAS-102 is larger than regorafenib, but if you tolerate regorafenib, if you have a patient where you think you should use it, I think the sequence is better, regorafenib before TAS-102.

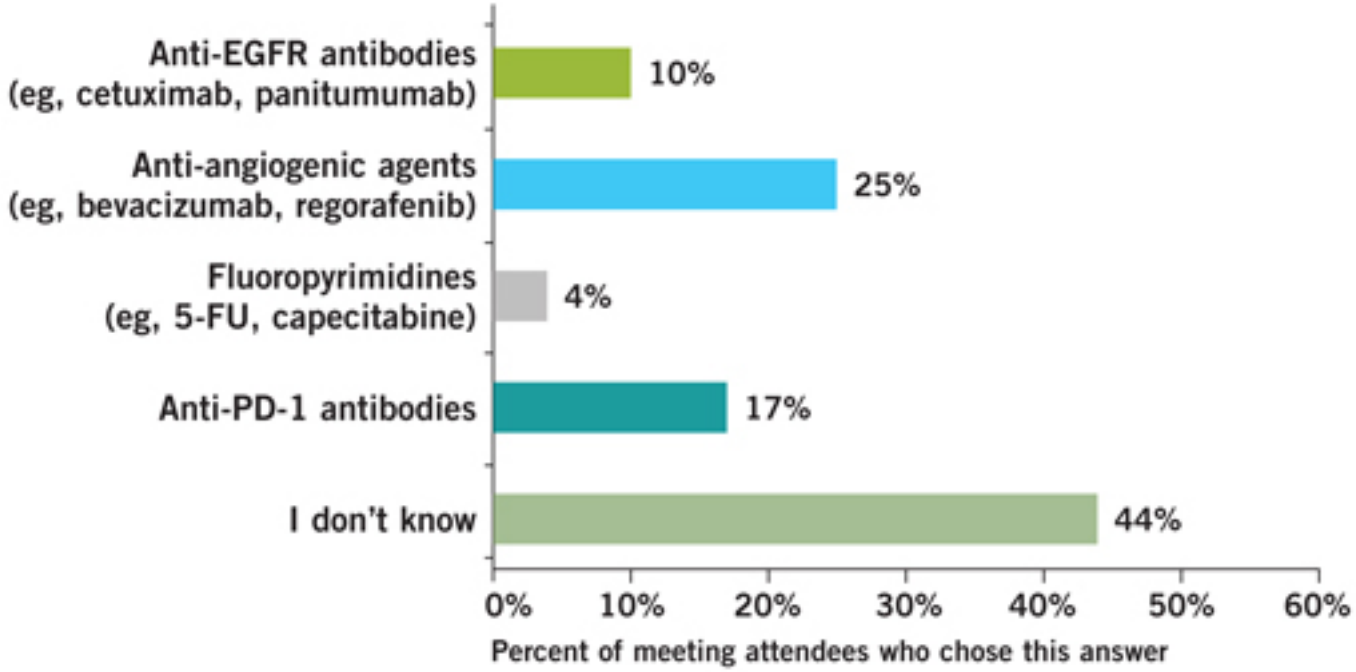
DR LOVE: Johanna, sometimes it's so hard just to look at data and figure out what that means in terms of patients. When you start either one of these drugs — as you say, you think they're about similarly effective — what do you think the chance is they're going to benefit? Maybe you can't show tumor shrinkage, but there's something about it. They were progressing. Now they're not. Is it a third? Is it 10%? Is it half?

DR BENDELL: Honestly — and this is just anecdotal — I would be guessing about 1 in 10 patients is going to benefit.

DR LOVE: That's pretty low. Axel?

DR GROTHEY: I think it's higher. We had 49 patients in the TAS-102 expanded access program. We saw benefit in about 30% of patients in terms of disease stabilization. We just looked at the efficacy data. Regorafenib is about 40%. It's very comparable. The critical time point is the scan at 8 weeks. Scan at 8 weeks really determines whether patients will have a benefit or not.

In patients with mCRC, central tumor necrosis observed radiologically in association with clinical benefit has been reported with...



DR LOVE: I heard about something earlier this year. I ask a million people about anti-angiogenics, and I never heard this before. I was curious about the audience. And it looks to me like a lot of the audience hadn't heard it. Eric Van Cutsem had this case, and you see these central tumor necrosis things in the lung. And I'm like, "What's that?" He goes, "Oh, yeah. You see that with anti-angiogenics." Is that the case? And do you see that with regorafenib? And, if you see it, does that mean the patient's going to do better?

DR GROTHEY: Yes, yes and yes. Yes, we see it with anti-angiogenesis agents — bevacizumab/regorafenib. We published a paper at ESMO GI this year about this. When you see cavitations in lung metastases on regorafenib, it's a better prognostic indicator. Those patients have a higher chance to benefit. It's not the perfect biomarker. It's an on-treatment marker. Those patients just do better.