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Integrating Clinical Insights: Key G/GEJ Cancer Data Analyzed from the San Diego Oncology Conference

Announcer:
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Dr. Klempner:
Hello. My name is Sam Klempner, GI Medical Oncologist from Mass General in Boston, and I'm here to recap some interesting news relevant to gastric and esophageal cancers from the recent AACR annual meeting.

I think the theme continues to be biomarker selection, and this is a great thing for patients. We're starting to catch up to some other cancers where they have more therapies linked to specific targets. Perhaps some of the most relevant ones at AACR were Claudin 18.2, and TROP2, and then we saw another bispecific dual checkpoint block inhibitor with PD-1 and CTLA-4.

Taking a step back and looking at the field, I think this highlights the advances that both we're making scientifically in terms of target identification, understanding heterogeneity of targets, understanding how we need to target both of these heterogeneous populations, probably to achieve maximal efficacy. And if you look at the strategies that are emerging in gastroesophageal cancer, many of them are building along this biologic observation. For example, we've seen bispecific antibodies targeting EGFR MET with the cytotoxic payload, we see TROP2 antibody from Merck, which was an encouraging clinical abstract highlighting response rates in the 20s% range across heavily pretreated so second and later than third-line patients. This sets the foundation for future phase 3 trial with TROP2 targeting in gastroesophageal adenocarcinomas, and continues to highlight the technological advances of antibody drug conjugate development, where we feel like we can actually achieve pretty good cytoreduction by both having a target where we can land the antibody, but also leveraging the bystander effect. So there's a lot of antibody conjugate development around linkers and payloads and optimizing the balance between need for target and payload efficacy and linker properties. And this will certainly continue to emerge, and is a very exciting area for patients.

One of the other antibody-based strategies that's interesting is BiTE antibodies, or CD3 engagers. And we saw a preclinical abstract primarily looking at a CD3 by Claudin 18.2 T-cell engager. And this is, of course, directly approximating tumor expressing – tumor cells expressing the target of Claudin 18.2 and adjacent T-cells. There are multiple companies developing CD3 by claudin engagers, including Astellas as well, the makers of zolbetuximab, which, again, we expect to be the first claudin therapy available on the market, hopefully in the coming months. It was just recently approved in Japan, so we expect global regulatory bodies may follow suit in the near future.

And finally, as many of the listeners know, there is a large body of literature looking at advances of moving immune checkpoint inhibitors into the frontline setting for gastric and esophageal squamous cell cancers and adenocarcinomas. We've seen some seminal trials like CheckMate 649 and KEYNOTE-859, and at AACR this year, we saw another important dataset, this time from a Chinese company, looking at chemotherapy alone in the control arm, versus chemotherapy plus the PD-1/CTLA-4 bispecific. And I think, although this data is hard to put in context without a PD-1-containing control arm, we can conclude a few observations that there was definitely an efficacy

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signal improvement upon chemotherapy alone, there were some quite durable responses, and the safety profile is consistent with these agents, suggesting that, you know, this is a feasible regimen.

And so these were probably the most clinical proximal updates from AACR. There were certainly a lot of additional abstracts and excellent educational sessions surrounding some of the biology underpinning these therapies. But for this audience, I think the therapeutic relevance is probably the most important.

So I hope this was relevant for everybody, and look forward to the next time we can all connect.

Announcer:
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