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### Current unmet needs in the field of unresectable HCC

#### Announcer:

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#### Dr. Abou-Alfa:

This is CME on ReachMD and I'm Dr. Ghassan Abou-Alfa from Sloan Kettering, New York.

#### Dr. He:

Hi, this is Dr. Ruth He from Georgetown University Hospital from Washington, DC.

#### Dr. Abou-Alfa:

Although significant progress has been made in recent years in the field of unresectable hepatocarcinoma, or HCC, many unmet needs remain. Ruth, can you please share your thoughts on some of these unmet needs in unresectable HCC?

#### Dr. He:

Yeah. In the last couple of years, we've shown huge progress made and because of that, we've had many frontline options, and I think, physicians sometimes can be confused about the lines of therapy and what to use, and also try to follow the guideline. And some of the patients do not get the adequate treatment according to the guidelines.

Ghassan, what are some of other unmet needs, in unresectable HCC?

#### Dr. Abou-Alfa:

Thank you, Ruth. I totally agree with you, a lot of choices now. But understandable, the choices can be confusing. For that reason, we might wonder about, shall we have some predictive biomarkers in regard to therapy? Shall we look into resistant mechanisms, or shall we how to choose therapy?

We know very well that the checkpoint inhibitors, which are the primary therapy for HCC in first-line, will be dependent on the alterations or combinations of an anti-PD1 and PDL-1 plus some enhancer, being either anti-CTLA-4 or anti-VEGF, or the likes.

No doubt that we have seen that, number one, patients with hepatitis B might fare best with that therapy, but doesn't mean that said, this is the only patient who will fare best for that in regard to therapy. Everybody will benefit. But also, I've noticed that certain population, as you already have shown us as well, in regard to the CD4 CD8 cells, will no doubt be enhanced outcome, if there was a CD8 which is high, CD4 low, as we have seen with the AZ22 study that preceded the HIMALAYA study.

#### Dr. He:

I agree with you. I think, right now, we don't really have a validated biomarker that would recommend to patients which combination we should use. I think with biomarker, it's really unmet need.

#### Dr. Abou-Alfa:

So, we heard from both of us that number one, yes, the good news is that there are many choices of therapy. Number two is, it could be sometimes confusing. Number three, the checkpoint inhibitor therapies apply for everybody despite that, yes, we might see more benefit for certain populations versus the other like, for example, hepatitis B would fare better than hep C or also, the non-vital. But also, I have

noticed that ultimately, the alteration of the immune microenvironment can enhance the outcome, even though this is still in the works. We have noticed some of this observation, like in the AZ22 study that preceded HIMALAYA, but more to go.

In regard to the advent of the data from the perspective of the etiology, and how specifically, in the ipi-nivo surprisingly, the subgroup analysis showed a tad of improvement in favor of the hep C compared to hep B.

**Dr. He:**

It is very interesting subgroup analyses have shown some combinations show more benefit in certain HCCs with different etiology. And, although those benefit can be seen in patients with other etiology, and this subgroup analysis are very interesting, but I do believe that we need to have a large data set of follow-up, maybe prospective study, to evaluate this and to see if that will help us to make decisions on which treatment we should pick for patients with different etiology.

**Dr. Abou-Alfa:**

With this, our time is up. Thank you for a great discussion, Dr. He. And thanks for the audience for tuning in.

**Announcer:**

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