

# First-in-class HER3/EGFR antibody safe, with antitumor activity in patients with refractory epithelial cancers

2 June 2015

MEHD7945A, a dual-action antibody that targets two members of the epidermal growth factor receptor (EGFR) family, was found to be safe and showed clinical activity in some patients with locally advanced or metastatic refractory epithelial cancers, including cancers of the head and neck, according to phase I clinical trial data published in *Clinical Cancer Research*, a journal of the American Association for Cancer Research (AACR).

"MEHD7945A is a humanized IgG1 antibody that has the capacity to target two members of the EGFR family, EGFR [also known as HER1] and HER3," said José Baselga, MD, PhD, physician-in-chief and chief medical officer at the Memorial Sloan Kettering Cancer Center in New York.

Baselga, who is also president of the AACR, explained, "For about 20 years, we have been working on the hypothesis of targeting EGFR in epithelial cancers as a fruitful approach based on our understanding that dysregulated EGFR plays an important role in tumorigenesis. What we have learned since then is that there are other players in the EGFR family, such as HER3, which are functionally similar to EGFR and, therefore, have a significant role in tumor promotion. We felt it is important that we hit not just EGFR alone, but also target HER3, with the goal of achieving more durable responses."

Binding of growth factors to EGFR and HER3 in a cell leads to activation and downstream signaling to promote cell growth. Dysregulated EGFR and/or HER3 can lead to overactive signaling, causing [uncontrolled cell growth](#) and proliferation, as seen in a variety of epithelial cancers. MEHD7945A has two antigen-binding arms, and they bind to unique targets on HER3 and EGFR, thus inhibiting the activity of multiple cancer signaling pathways.

"In a phase I clinical trial, we found that MEHD7945A was well tolerated as a single agent, and we were able to confirm partial responses in [patients](#) who had refractory disease, which clearly suggests that this dual-targeting approach is a good strategy moving forward," Baselga added.

Baselga and colleagues enrolled 66 patients at six sites in the United States and Spain: 30 patients to the dose-escalation study and 36 to the dose-expansion study. All patients had received prior systemic therapies, and about 50 percent of them had received prior anti-EGFR therapies. Patients had incurable, locally advanced, or metastatic epithelial cancer, including colorectal, non-small cell lung, or head and neck cancers, which had progressed despite prior therapies.

Six different dose levels were tested in the dose-escalation study, and patients enrolled in the dose-expansion study received 14 mg/kg b.w. of the drug intravenously, every two weeks until patients experienced toxicity or disease progression.

No dose-limiting toxicities or drug-related grade 4 adverse events were reported in the dose-escalation or the dose-expansion cohorts. Two patients with squamous cell carcinoma of the head and neck (in the tongue and larynx, respectively) had partial responses, and eight patients had stable disease that lasted for 16 weeks or longer.

Patients whose tumors had high levels of the growth factor heregulin, which binds to EGFR, were found to benefit from the drug, according to Baselga. "Presence of high levels of the ligand [heregulin] could be a marker of response to this drug, but this needs further confirmation," he said.

"We have been using antibodies to treat cancers for a while now, but recent advancements in

technology are allowing us to use antibodies in a way we have not done in the past," Baselga noted. "Dual targeting of HER2 and HER3 was shown to be a promising strategy for breast cancers; this study adds further support to the dual-targeting approach, and also speaks to the increasing opportunities we all have with engineering antibodies for patient benefit."

**More information:** "Safety and Pharmacokinetics/Pharmacodynamics of the First-in-Class Dual Action HER3/EGFR Antibody MEHD7945A in Locally Advanced or Metastatic Epithelial Tumors." *Clin Cancer Res* June 1, 2015 21:2462-2470; DOI: [10.1158/1078-0432.CCR-14-2412](https://doi.org/10.1158/1078-0432.CCR-14-2412)

Provided by American Association for Cancer Research

APA citation: First-in-class HER3/EGFR antibody safe, with antitumor activity in patients with refractory epithelial cancers (2015, June 2) retrieved 1 June 2022 from <https://medicalxpress.com/news/2015-06-first-in-class-her3egfr-antibody-safe-antitumor.html>

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