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Subcutaneous Isatuximab Matches IV in Multiple Myeloma: Insights from IRAKLIA

Dr. Mimi Maeusli:
You're listening to *Project Oncology* on ReachMD, and this is an *Audio Abstract*. I'm Dr. Mimi Maeusli, and today, we're reviewing the findings from the large, phase 3 IRAKLIA trial, which was a randomized study evaluating a subcutaneous delivery option for patients with relapsed or refractory multiple myeloma. Published in the *Journal of Clinical Oncology*, this study compared subcutaneous isatuximab delivered via an on-body injector, or O-B-I for short, plus pomalidomide and dexamethasone against the standard IV isatuximab-based combination.

For some background, the study included 531 adult patients with relapsed and/or refractory multiple myeloma who had received at least one prior line of therapy, including lenalidomide and a proteasome inhibitor. Patients were randomly assigned 1:1 to receive isatuximab either intravenously at 10 mg/kg or the recommended phase 2 dose of 1,400 mg via subcutaneous O-B-I. Patients were stratified by multiple myeloma isotype of IgG or non-IgG, body weight, and prior number of therapies. All patients also received standard-dose pomalidomide and dexamethasone in four-week cycles.

At baseline, cohort characteristics were relatively balanced, with a slightly higher number of patients who were 75 years or older, with reduced eGFR, increased plasmacytosis, and stage III disease in the wearable device cohort.

Regarding the goals of the study, the coprimary endpoints were overall response rate and steady-state trough concentration. Key secondary endpoints included the rate of very good partial response or better, steady-state trough concentration at four weeks, incidence rate, and patient satisfaction of the administration route. Other secondary endpoints evaluated progression-free survival, duration of response, time to first and best response, safety, and tolerability.

Now, if we turn our attention to the results, the overall response rate was 71.1 percent and 70.5 percent for the subcutaneous and IV administration, respectively. The subcutaneous route proved noninferior to the IV infusion, achieving a relative risk of 1.008, which was above the 0.839 threshold. The steady-state trough concentration was 499 ug/mL for the subcutaneous group and 341 ug/mL for the IV group. Similarly, the subcutaneous route demonstrated noninferiority as it exceeded the threshold of 0.8, with a geometric mean ratio of 1.532. Upon stratification, similar results were also seen.

As for the secondary endpoints, 12-month progression-free survival was similar between groups as was the median time to first response of approximately two months. The median time to best response was 4.6 months for the subcutaneous cohort, compared with 3.9 months among those receiving IV treatment. In terms of very good partial or complete response rates, the subcutaneous O-B-I route demonstrated noninferiority with steady-state trough concentration compared to IV administration. And when it came to patient satisfaction, participants receiving the O-B-I route reported a higher degree of satisfaction at 70 percent compared to 53.4 percent in the IV group.

Additionally, a noticeable difference was seen in infusion reactions between the two cohorts as it was 1.5 percent for the subcutaneous O-B-I cohort and 25 percent for the IV cohort. The majority of infusion reactions were grade 1 or 2, which typically occurred during the first infusion. The O-B-I route was tolerable in that infusion reactions occurred in 19 of over 5,000 injections, with all except one infusion site reaction of grade 1 resolving in about a day.

In terms of safety, no new adverse event signals were reported with subcutaneous O-B-I. Pneumonia was the most common adverse event leading to treatment discontinuation in both groups, with pneumonia and sepsis reported as the most common adverse event that led to death in the IV cohort. And the most common nonhematologic adverse event, regardless of grade, was upper respiratory tract

infection.

So to sum up all of these findings, the IRAKLIA trial confirms that subcutaneous isatuximab delivered via on-body injector is noninferior to IV in both efficacy and safety, and it may even offer added benefits in time savings, convenience, and patient satisfaction. As new delivery models emerge, this study reinforces the growing focus on *how* care is delivered, and not just on *what* we deliver.

This has been an *Audio Abstract* for *Project Oncology*, and I'm Dr. Mimi Maeusli. To access this and other episodes in our series, visit ReachMD dot com, where you can Be Part of the Knowledge. Thanks for listening!

Reference

Ailawadhi S, Špička I, Spencer A, et al. Isatuximab Subcutaneous by On-Body Injector Versus Isatuximab Intravenous Plus Pomalidomide and Dexamethasone in Relapsed/Refractory Multiple Myeloma: Phase III IRAKLIA Study. J Clin Oncol. Published online June 3, 2025. doi:10.1200/JCO-25-00744