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Modern Era, New Outcomes: Survival Trends in Breast Cancer Brain Metastases

Mr. Quigley:

You're listening to *Project Oncology* on ReachMD, and this is an *AudioAbstract*. I'm Ryan Quigley, and today, we're diving into a major question in metastatic breast cancer: How are patients with brain metastases doing in the modern treatment era?

And now, thanks to one of the largest single-center reviews to date out of UCSF, we have a clearer picture of how things have changed over the past 25 years.

So let's set the stage. The team looked back at 507 patients treated between 1997 and 2024. All patients in the study had metastatic breast cancer and developed parenchymal brain metastases, which are within the brain tissue itself. To find these patients, researchers combed through radiation oncology records, clinical databases, and pathology reports and then manually gathered details about tumor biology, treatments, and survival.

The median age at the time of metastatic diagnosis was 53. And the major subtypes were all represented:

- HR positive, HER2 negative at 36 percent,
- HER2 positive at 39 percent, and
- Triple negative breast cancer, or TNBC, at about 25 percent.

Most patients—around 75 percent—already had extracranial metastases when their brain metastases were discovered. And two-thirds had multiple brain lesions rather than just one. Additionally, nearly 19 percent eventually developed leptomeningeal disease, or LMD—a complication the study later shows is strongly tied to worse outcomes.

The treatment landscape for brain metastases has changed dramatically in this 25-year window. Before patients were diagnosed with brain metastases, they'd typically received one line of therapy. That reflects the earlier era, when far fewer therapies had meaningful CNS activity.

But after the brain metastases, nearly every patient received some form of CNS-directed radiation. About a third underwent brain metastasis surgery. And depending on their subtype, many patients were treated with modern therapies like tucatinib, T-DXd, T-DM1, abemaciclib, sacituzumab govitecan, and various checkpoint inhibitors.

These are drugs we now know can reach the brain—or at least meaningfully impact CNS disease—and they likely play a major role in the improvement in survival seen in recent years. Across the entire cohort, the median real-world overall survival from the time of brain metastasis diagnosis was 21.6 months. But the subtypes tell a much more nuanced story:

- HER2 positive disease came out on top with a median survival of 31 months.
- HR positive, HER2 negative patients lived about 19.6 months.
- And patients with TNBC had the shortest survival at 12.8 months.

But the most compelling part of this study is the comparison between two eras:
1997 to 2014 versus 2015 to 2024. HER2 positive and TNBC patients saw significant survival improvements in the modern era.

- For HER2 positive, survival jumped from 26.2 months to 41.2 months.
- For TNBC, it doubled from 7.0 to 14.9 months.

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On the other hand, HR positive, HER2 negative patients didn't experience the same gains. Their outcomes remained essentially unchanged—one of the biggest unmet needs highlighted by the study.

Multivariable analysis helped clarify which factors have the strongest impact on survival. Factors tied to longer survival included:

- Having HER2 positive disease,
- Undergoing surgical resection of brain metastases,
- And being diagnosed after 2014

Factors associated with shorter survival included:

- Being diagnosed with TNBC,
- Having 6–10 brain metastases,
- Having extracranial metastatic disease,
- And developing leptomeningeal disease.

So what does all this mean? We're seeing real, measurable progress—especially for HER2 positive disease and, more recently, for TNBC. Advances in systemic therapies with CNS activity are making a tangible difference.

But for HR positive, HER2 negative patients with brain metastases, the needle hasn't moved in the same way. And that's a signal loud and clear: this group needs better CNS-penetrant strategies and much more attention in therapeutic development.

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

Reference

Krasnow NA, Jayaraj M, Salans M, et al. Evaluating survival trends over time in patients with metastatic breast cancer and brain metastases: a single center retrospective cohort study. *Breast Cancer Res*. 2025;27(1):191. Published 2025 Oct 28. doi:10.1186/s13058-025-02121-7

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