

## DEBBRAH

### Trastuzumab Deruxtecan in patients with HER2[+] or HER2-Low Advanced Breast Cancer and Pathologically Confirmed Leptomeningeal Carcinomatosis: Results from Cohort 5 of the DEBBRAH Study

#### Context

Leptomeningeal carcinomatosis is a rare but serious complication that happens when advanced cancer spreads to the cerebrospinal fluid and leptomeninges (the membranes that surround the brain and spinal cord). It occurs in approximately 10% of patients with advanced breast cancer. It is often associated with a poor patient outcome due to the limited therapeutic options available. Currently, there are no specific drugs approved for metastatic breast cancer patients with brain metastases and/or leptomeningeal carcinomatosis, and there is no consensus on how to manage these cases. In addition, clinical trials commonly exclude these patients. This means that the results of these trials may not apply to them, and the potential benefits of new treatments may be missed.

## About DEBBRAH and the patients

The DEBBRAH trial has been designed to address this gap in knowledge. It aims to investigate whether an antibody-drug conjugate called trastuzumab deruxtecan, which has shown promise in treating breast cancer that has spread to the brain and elsewhere in the body, can help improve the treatment for this specific group of patients.

The DEBBRAH phase II trial was designed to evaluate the efficacy and safety of trastuzumab deruxtecan in patients with HER2[+] and HER2-low advanced breast cancer (meaning that tumors were characterized by the presence of either high or low levels of HER2 protein) with a history of brain metastases and/or leptomeningeal carcinomatosis. Patients were enrolled into one of five cohorts based on the HER2 protein level and type of central nervous system involvement. Here, we report the results of cohort 5, which specifically included patients with leptomeningeal carcinomatosis. The main objective for this cohort was to measure the amount of time from the start of the treatment until to death from any cause, also known as overall survival.

A total of 7 patients with leptomeningeal carcinomatosis were included in the cohort 5 and were followed-up for 12 months (range, 2.5-18.6). The median age was 57 years (range, 42-69). The patients were given 5.4 mg/kg trastuzumab deruxtecan intravenously once every 21 days. As of April 4, 2023, two (28.6%) patients were still receiving treatment after 18.6 and 12.0 months, respectively. The results show that treatment with trastuzumab deruxtecan led to a remarkable median overall survival of 13.3 months, meeting the primary endpoint. Five (71.4%) patients experienced a prolonged stabilization of their disease for at least 24 weeks, and the median time before their disease worsened again (known as progression free survival), was 8.9 months. The safety profile was consistent with previous studies.

## Conclusions

In conclusion, trastuzumab deruxtecan showed promising activity with no new safety concerns in patients with HER2[+] and HER2-low breast cancer who had not received previous treatment for leptomeningeal carcinomatosis. These encouraging data warrant further investigation to address the unmet need in this difficult-to-treat disease.

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### ABOUT MEDSIR

Founded in 2012, MEDSIR works closely with its partners to drive innovation in oncology research. Based in Spain and the United States, the company manages all aspects of clinical trials, from study design to publication, utilizing a global network of experts and integrated technology to streamline the process. The company offers proof-of-concept support and a strategic approach that helps research partners experience the best of both worlds from industry-based clinical research and investigator-driven trials. To promote independent cancer research worldwide, MEDSIR has a strategic alliance with Oncoclínicas, the leading oncology group in Brazil with the greatest research potential in South America.

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**Trastuzumab Deruxtecan in patients with HER2[+] or HER2-Low Advanced Breast Cancer and Pathologically Confirmed Leptomeningeal Carcinomatosis: Results from Cohort 5 of the DEBBRAH Study**

## **-Thank you-**

If you participated in this study, MEDSIR, would like to thank you for your participation.

This summary will describe the study results.

If you have any questions about the study or the results, please contact the doctor or staff at your study site.

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## About the study

Leptomeningeal carcinomatosis is a rare but serious complication that happens when advanced cancer spreads to the cerebrospinal fluid and leptomeninges (the membranes that surround the brain and spinal cord). It occurs in approximately 10% of patients with advanced breast cancer. It is often associated with a poor patient outcome due to the limited therapeutic options available. Currently, there are no specific drugs approved for metastatic breast cancer patients with brain metastases and/or leptomeningeal carcinomatosis, and there is no consensus on how to manage these cases. In addition, clinical trials commonly exclude these patients. This means that the results of these trials may not apply to them, and the potential benefits of new treatments may be missed.

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## DEBBRAH Trial



<b>Intervention</b>  Trastuzumab Deruxtecan	<b>Cohorts</b> <b>Cohort 1:</b> HER2+ with non-progressing BM <b>Cohort 2:</b> HER2+ or HER2 low expressing with asymptomatic untreated BM <b>Cohort 3:</b> HER2+ with progressing BM after local treatment <b>Cohort 4:</b> HER2 low expressing with progressing BM after local treatment <b>Cohort 5:</b> HER2+ or HER2 low expressing with leptomenigeal carcinomatosis
<b>Patient population</b>  HER2+ advanced breast cancer with BM and/or leptomenigeal carcinomatosis  N = 39	
<b>Preliminary Results</b>	<b>Cohort 1:</b> 87% with stable brain mets and without progressive disease at 16 weeks <b>Cohort 3:</b> ORR-IC in 4 patients, 1 with stable disease at 24 weeks

### About the patients who participated

A total of 7 patients with leptomenigeal carcinomatosis were included in the cohort 5 and were followed-up for 12 months (range, 2.5-18.6). The median age was 57 years (range, 42-69). The patients were given 5.4 mg/kg trastuzumab deruxtecan intravenously once every 21 days. As of April 4, 2023, two (28.6%) patients were still receiving treatment after 18.6 and 12.0 months, respectively.

## What were the results of the study?

The results show that treatment with trastuzumab deruxtecan led to a remarkable median overall survival of 13.3 months, meeting the primary endpoint. Five (74.1%) patients experienced a prolonged stabilization of their disease for at least 24 weeks, and the median time before their disease worsened again (known as progression free survival), was 8.9 months. The safety profile was consistent with previous studies.

## Medical Conclusions

Treatment with T-DXd in patients with HER2[+] or HER2-low ABC and LMC led to a remarkable median OS of 13.3 months, meeting the primary endpoint. No objective responses were observed, but five (74.1%) patients achieved a prolonged stabilization ( $\geq 24$  weeks) for an overall clinical benefit rate of 71.4% and a median progression free survival of 8.9 months.

## Patient Conclusions

Leptomeningeal carcinomatosis is a devastating complication that is associated with a poor prognosis due to the limited available therapeutic options. The results of the DEBBRAH trial are extremely interesting and suggest that leptomeningeal carcinomatosis may become a more treatable condition with the introduction of new HER2-targeted agents.



## Where I can find more information about the study?

Your doctor can help you understand more about this study and the results. Speak to your doctor about the treatment options available in your country. You should not make changes to your care based on the results of this or any single study. Keep taking your current treatment unless instructed by your doctor.

For more details, please visit:

<https://www.medsir.org/debbrah-clinical-trial>

The full scientific report of this study is available online at:

[www.clinicaltrials.gov](http://www.clinicaltrials.gov)

Use the study identifier  
NCT04420598

Again, we would like to thank the patients who contributed to this study.

The content for this document was finalised by MEDSIR on the 9th of November of 2023. The information in this summary does not include additional information available after this date.

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