PONTIAC

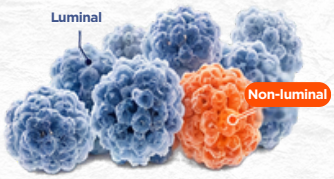
A randomized phase II study of trastuzumab deruxtecan versus CDK4/6 inhibitor-based endocrine therapy as first-line treatment in patients with HR-positive, HER2-low or ultralow breast cancer.



1 THE UNMET NEED

Not all HR-positive breast cancers are biologically the same

Some HR-positive tumors have a non-luminal molecular profile and may be less sensitive to endocrine-based treatment.



Identifying these patients upfront could help choose a more effective first-line strategy.

2 STUDY DESIGN

- Planned N: 200 patients
- International, multicenter
- Randomized phase II
- 1:1 randomization
- Open-label

RANDOMIZATION 1:1

T-DXd	Endocrine Therapy + CDK4/6 Inhibitor
5.4 mg/kg IV every 3 weeks	Investigator's choice of CDK4/6 Inhibitor

Primary Endpoint
Progression-Free Survival (PFS)

Key secondary endpoints: overall survival, objective response rate, clinical benefit rate, duration of response, time to response, health-related quality of life, and safety.

3 WHAT MAKES PONTIAC DIFFERENT

Conventional approach	PONTIAC approach
HR-positive HER2-low/ultralow	HR-positive HER2-low/ultralow
	PAM50 molecular subtyping
	Non-luminal biology
Treatment decision	Treatment strategy under investigation

4 FEATURES THAT MAY PROMPT PRE-SCREENING

For endocrine-sensitive disease, features that may prompt early pre-screening consideration include:

- **ER ⩽ 50%** Lower ER expression
- **Ki-67 >50%** High poliferative activity
- Known local non-luminal PAM50 result
- Liver metastases

5 WHO MAY BE CONSIDERED FOR PONTIAC?

Adults with HR-positive, locally recurrent inoperable or metastatic breast cancer, no prior systemic therapy for advanced disease, centrally confirmed HER2-low or ultralow disease, and a non-luminal intrinsic subtype confirmed by central PAM50 analysis.

6 POTENTIAL IMPACT IF PONTIAC IS POSITIVE

It could help identify patients who may benefit from a different treatment approach from the start.

It could strengthen the evidence for using intrinsic molecular subtype to guide first-line treatment selection.

It could help refine first-line treatment selection beyond conventional receptor status.

Can a deeper understanding of tumor biology help refine first-line treatment selection from the start?

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