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congress

ESG401, a novel Trop2 antibody-drug conjugate (ADC), and its efficacy evidence in HER2-negative metastatic breast cancer with brain metastases

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Declaration of Interests

Fei Ma

No conflicts of interests to disclose.

Background

■ Brain Metastases (BMs) in mBC:

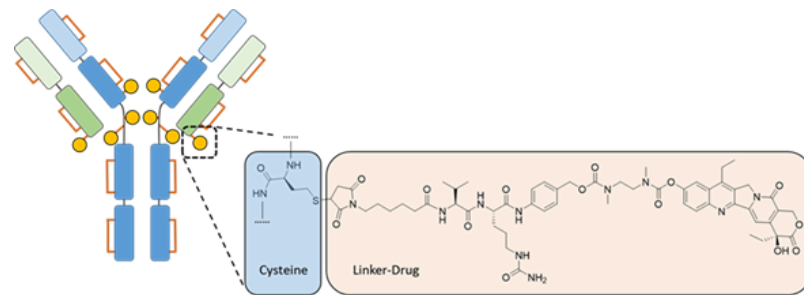
- Affect 16–30% of patients^{1,2};
- Associated with higher mortality and poorer prognosis^{1,3};
- Need for new treatments⁴

■ ESG401:

- Novel ADC targeting TROP2, linked to SN-38
- Suppresses BMs in preclinical models
- Preliminary safety and efficacy were validated in early clinical trial

■ ESG401-101 Trial:

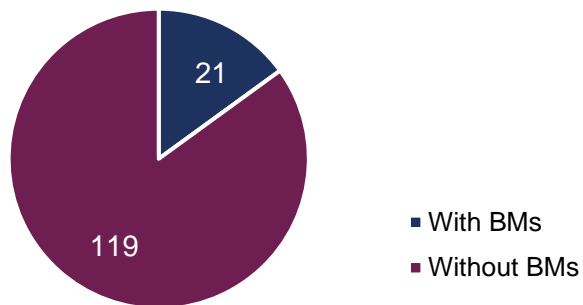
- Open-label, multi-dose, Phase Ia/Ib
- Enrolled patients with stable or newly developed brain metastases



1. Rostami R, et al. *J Neuro-oncol.* 2016;127(3):407-414. 2. Chen Q, et al. *Front Oncol.* 2023;12:1086821. 3. Li Y, et al. *Breast.* 2021;55:30–6. 4. Kadamkulam Syriac A, et al. *Breast Cancer.* 2022;14:1–13.

Patient Characteristics

- A total of 140 HER2-negative mBC pts were enrolled.



Dose group	Patients with efficacy-evaluable BMs
12 mg/kg ^a	6
14 mg/kg ^a	4
16 mg/kg ^a	7
Total	17

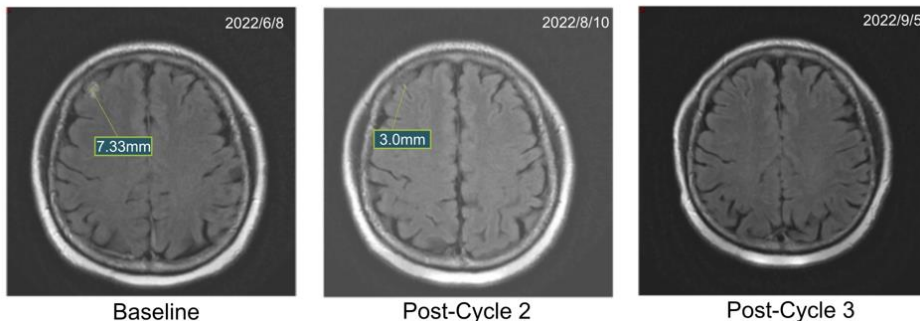
^a Dosing regimens: Days 1, 8, and 15 in a 28-day cycle

Patient characteristics	ESG401-101 (n=21)
Age, median (range), years	50.5 (35-69)
Gender	
Female	21 (100)
ECOG PS, n (%)	
0	3 (14)
1	18 (86)
Subtypes	
TNBC	14 (67)
HR+/HER2-	7 (33)
SOD of Brain lesion median (range), mm	8 (3-21.17)
Prior treatments, n (%)	
Radiotherapy only	2 (10)
Operation only	1 (5)
Radiotherapy+Operation	0
Radiotherapy+Operation+Capecitabine	0
Untreated	18 (86)

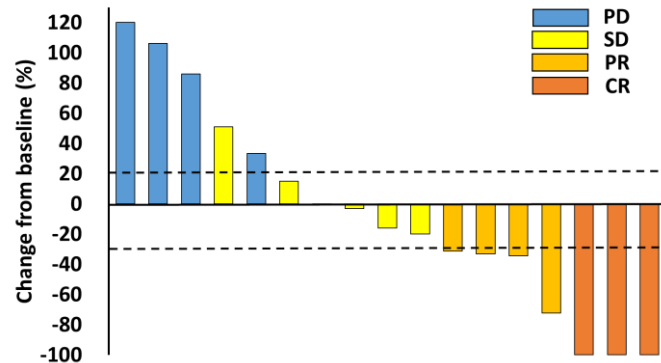
Efficacy Summary

Response	Patients with BMs
IC-ORR % (95% CI)	41% (18.4-67.1%)
IC-DCR % (95% CI)	76% (50.1-93.2%)
ORR % (95% CI)	53% (27.8-77.0%)
DCR % (95% CI)	71% (44.0-89.7%)
Median PFS, months (95% CI)	4.6 (2.0, 9.8)

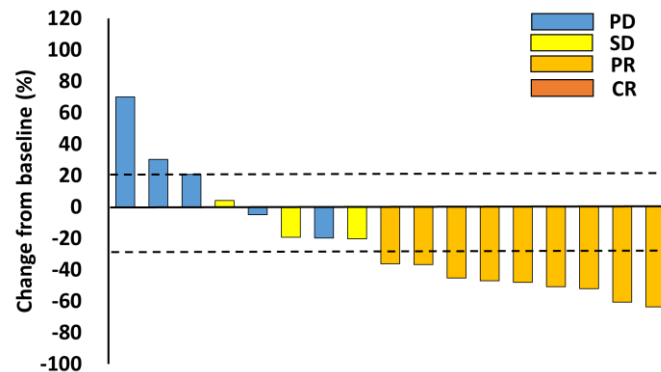
Reduction in the size of the intracranial lesions in Patient #0101009



- **BOR:** 3 pts achieved a complete intracranial response (IC-CR).
- **Tx Duration:** Longest ESG401 tx duration: 21.3 mo (ongoing).



Waterfall plot of best percent change in SOD in brain lesions



Waterfall plot of best percent change in SOD in target lesions

Safety Summary

- The most common grade ≥ 3 TRAEs is neutropenia and leukopenia.
- The safety profile of ESG401 is consistent in patients with and without BMs.

TRAEs	All patients (n=21), n (%)	
	Any Grade*	Grade ≥ 3
Leukopenia	17 (81.0)	9 (42.9)
Neutropenia	16 (76.2)	9 (42.9)
Anemia	12 (57.1)	0
Nausea	8 (38.1)	0
Vomiting	8 (38.1)	0
Fatigue	7 (33.3)	0
Diarrhea	5 (23.8)	0
Elevated alanine aminotransferase	5 (23.8)	0
Thrombopenia	5 (23.8)	1 (4.8)
Decreased appetite	4 (19.0)	0

*TRAEs of any grade occurring in $\geq 10\%$ of patients are listed.

Conclusion

- **ESG401 shows promising therapeutic efficacy in HER2-negative metastatic breast cancer patients, with and without BMs.**
- **ESG401 demonstrates clear and encouraging efficacy in treating BMs, with consistent responses in both intracranial and extracranial lesions.**
- **ESG401 has a manageable safety profile, consistent in patients with and without BMs.**
- **These findings are being further evaluated in ongoing phase 3 studies.**

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