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Results from a Phase Ia/Ib Study of ESG401, a Novel Trop2 Antibody-Drug Conjugate, in Patients with Different Subtypes of Metastatic Breast Cancer

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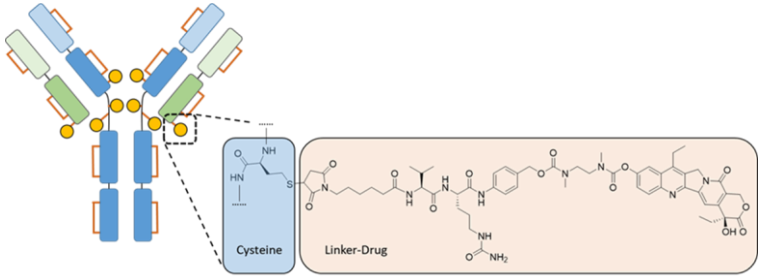
Declaration of Interests

Fei Ma

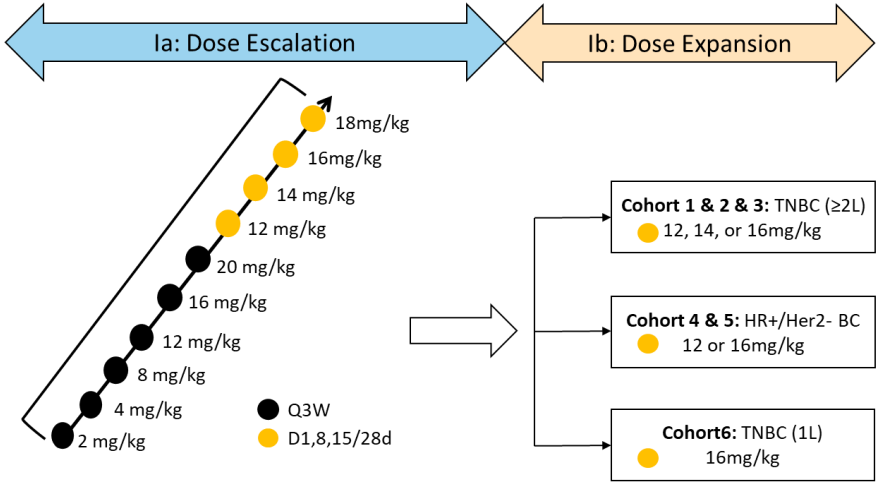
No conflicts of interests to disclose.

Introduction and Study Design



- **ESG401:** a novel ADC comprising a humanized anti-TROP2 IgG1 monoclonal antibody conjugated to SN-38 with a **DAR of 8** and a **stable cleavable linker.**

- **ESG401-101**: an open-label, multiple-dose, dose-escalation, and cohort expansion Phase Ia/ Ib trial enrolled pts with metastatic solid tumors, focusing on metastatic breast cancer.



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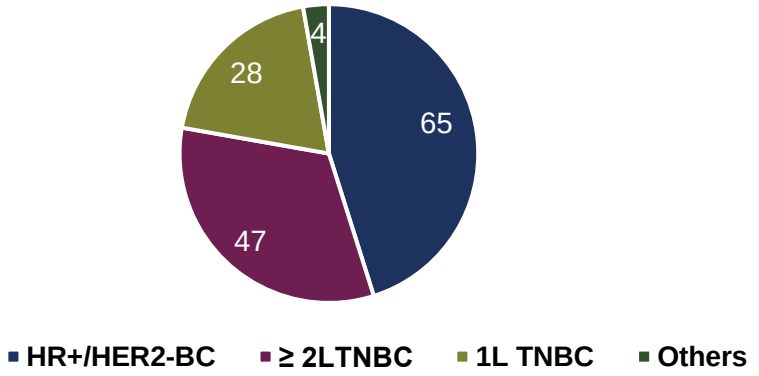
Patient Characteristics

Patient characteristics	ESG401-101 (n=144[a])
Age, median (range), years	52 (32-73)
ECOG PS, n(%)	
0	44 (31)
1	100 (69)
De novo metastatic disease, n (%)	
Yes	23 (16)
No	121 (84)
Visceral metas at baseline, n (%)	126 (88)
Brain metastatic disease	21 (15)
Liver metas	85 (59)
Lung metas	75 (52)
Prior therapies in metastatic setting, median (range)	2 (0-12)
≥2 prior lines of therapy, n (%)	105 (73)
≥5 prior lines of therapy, n (%)	28 (19)
Median time from diagnosis of metastatic disease to enrollment (range), mo	18.1 (0.3-147.0)

Patient characteristics	ESG401-101 (n=144[a])
Previous systemic treatment, n (%)	
Taxanes	132 (92)
Anthracyclines	109 (76)
Platinum-based chemotherapy	58 (40)
Immunotherapy	26 (18)
Other ADC	6 (4)

[a] Including 40 patients in Phase 1a and 104 patients in Phase 1b.



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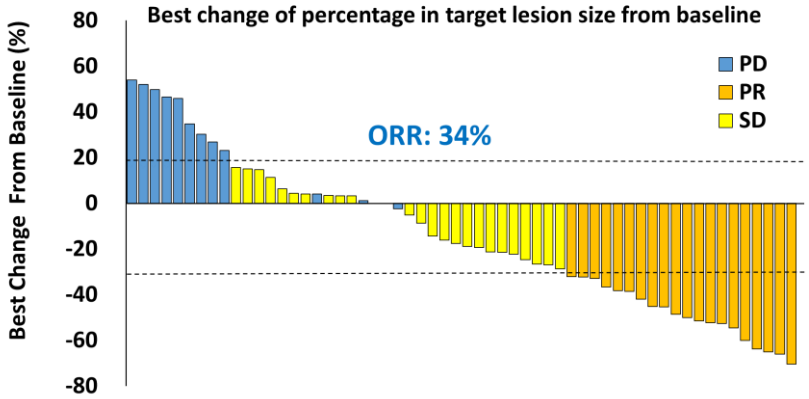
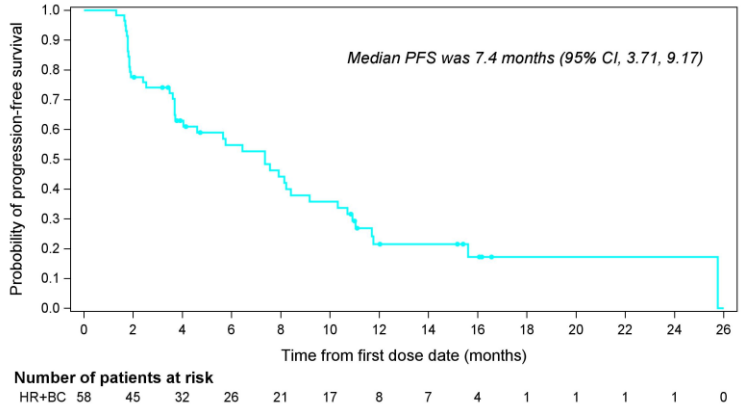
Efficacy of ESG401 in Late-stage HR+/HER2-BC

Patient characteristics	HR+/HER2-BC (n=65[a])
Visceral metas at baseline, n (%)	60 (92)
Brain	7 (11)
Liver	48 (74)
Lung	26 (40)
Prior CDK4/6 inhibitor use, n (%)	51 (78)
Endocrine resistance, n (%)	62 (95)
Primary	33 (51)
Secondary	29 (45)

Parameters	HR+/HER2-BC (n=58[b])
ORR, n (%)	20 (34)
Confirmed CR/PR	17 (29)
DCR, n (%)	45 (78)
DoR	
Medican (Range), mo	8.0 (4.6, 23.9)
6-mon DoR rate, %(95%CI)	70.0 (49.9, 90.1)
PFS	
Medican (Range), mo	7.4 (3.7, 9.2)
6-mon PFS rate, %(95%CI)	54.7 (41.4, 68.0)

a. All patients; b. Efficacy-evaluable patients





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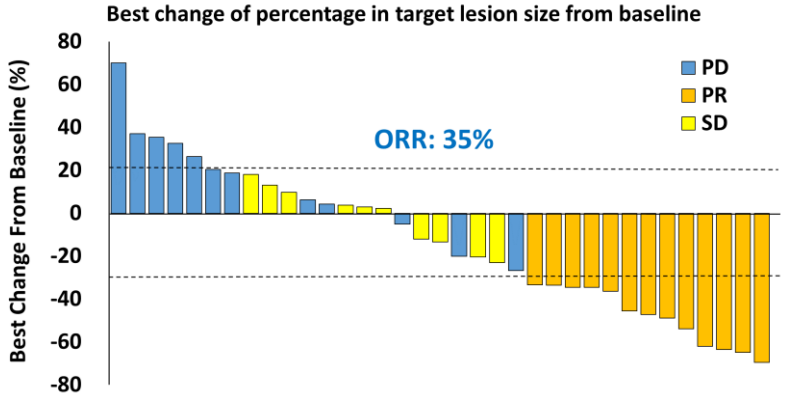
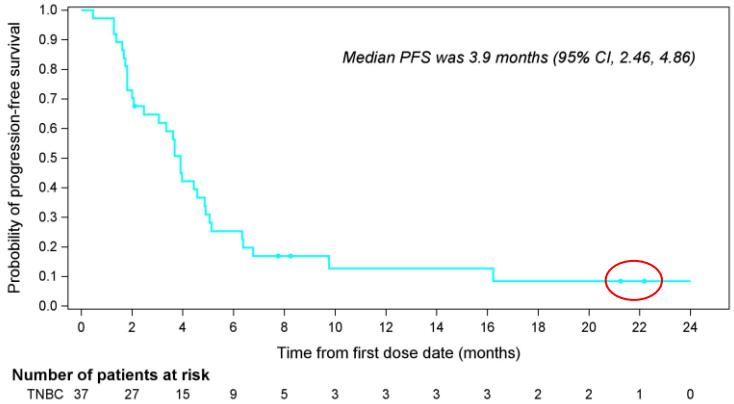
Efficacy of ESG401 in Late-stage TNBC

Patient characteristics	TNBC (n=47[a])
Visceral metas at baseline, n (%)	41 (87)
Brain	11 (23)
Liver	25 (53)
Lung	32 (68)
Prior therapies in metastatic setting, median (range)	3 (1-12)
≥2 prior lines of therapy, n (%)	42 (89)
≥3 prior lines of therapy, n (%)	27 (57)

Parameters	TNBC (n=37[b])
ORR, n (%)	13 (35)
Confirmed CR/PR	10 (27)
DCR, n (%)	23 (62)
DoR	
Medican (Range), mo	4.5 (3.1, 13.6)
6-mon DoR rate, %(95%CI)	38.5 (12.0, 64.9)
PFS	
Medican (Range), mo	3.9 (2.5, 4.9)
6-mon PFS rate, %(95%CI)	25.3 (11.1, 39.6)

a. All patients; b. Efficacy-evaluable patients





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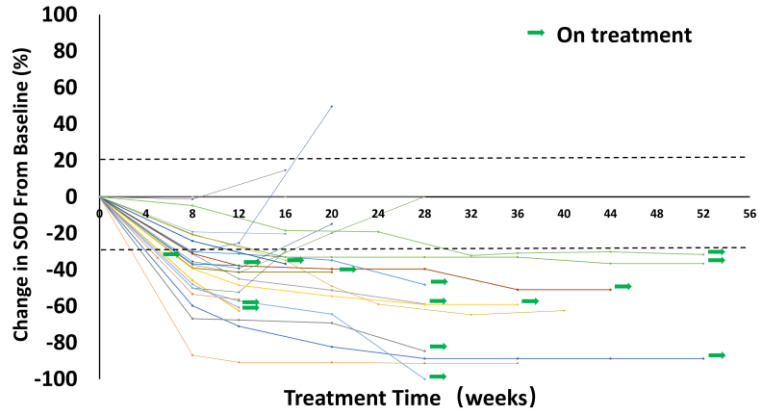
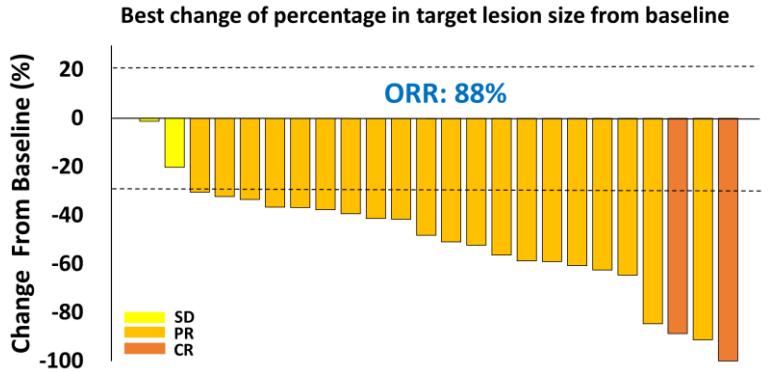
Efficacy of ESG401 in First-line TNBC

Patient characteristics	TNBC (n=28[a])
ECOG PS, n (%)	
0	10 (36)
1	18 (64)
Visceral metas at baseline, n (%)	21 (75)
Lung	14 (50)
Bone	12 (43)
Liver	11 (39)
Brain	3 (11)

Parameters	TNBC (n=25[b])
ORR, n (%)	22 (88)
Confirmed CR/PR	19 (76)
DCR, n (%)	25 (100)
DoR	
Medican (Range), mo	Not reached
PFS	
Medican (Range), mo	Not reached

a. All patients; b. Efficacy-evaluable patients





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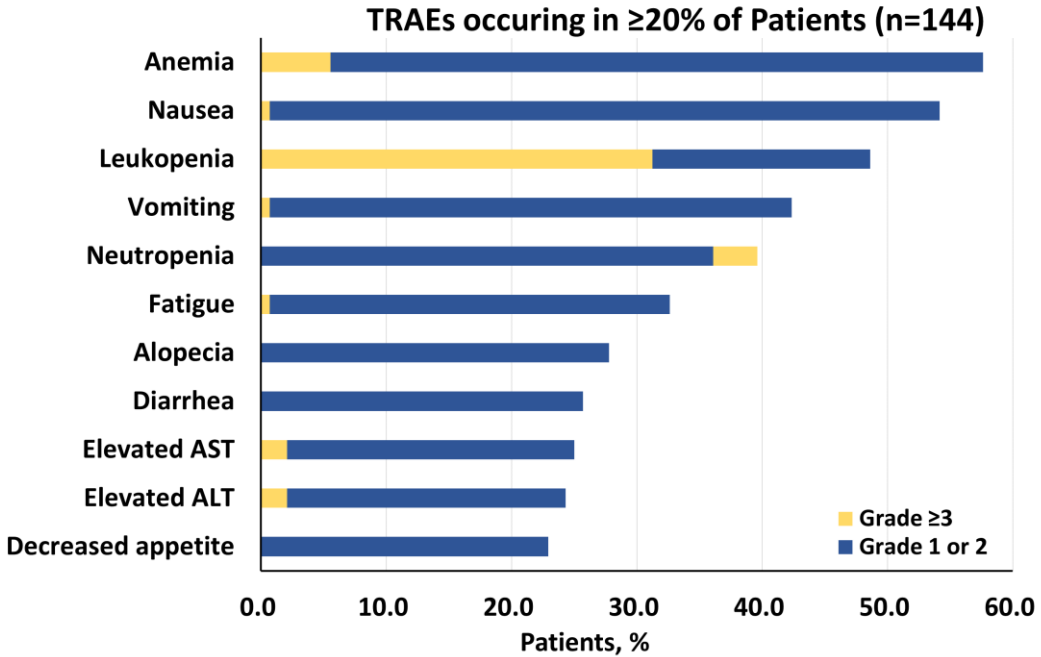
Overview of Safety

- The most common grade ≥3 TRAEs were neutropenia and leukopenia.
- No grade ≥3 diarrhea, rash, or interstitial lung disease was observed.

Events	All patients, n (%) (n=144)
TRAEs	141 (97.9)
Grade ≥3 TRAEs	69 (47.9)
Serious TRAEs	17 (11.8)
Leading to death	0
Leading to discontinuation	3 (2.1)
Leading to dose delay	55 (38.2)
Leading to dose reduction	9 (6.3)



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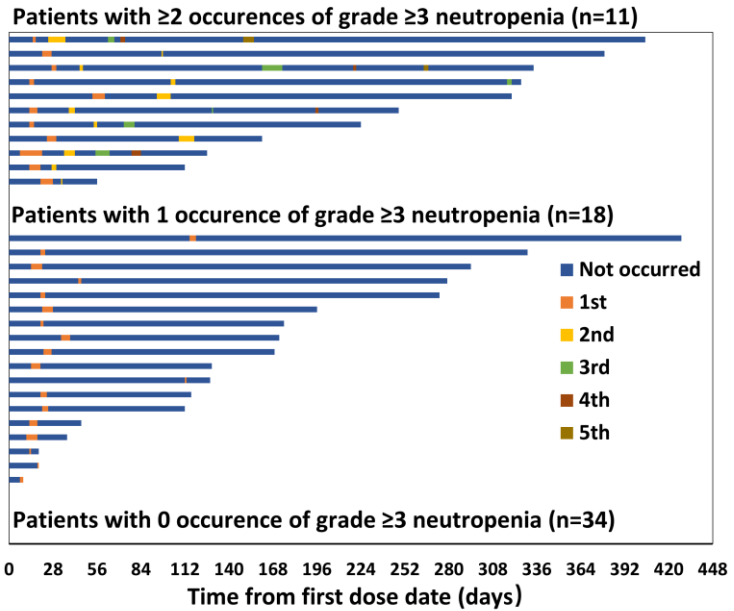
Overview of Grade ≥3 neutropenia

- Only 17.5% of subjects at 16mg/kg D1,8,15/28d had ≥2 occurrence of grade ≥3 neutropenia throughout the treatment.
- No grade ≥3 neutropenia caused permanent discontinuation; they were manageable, and subjects recovered after treatment.

Parameters	Grade ≥3 neutropenia (n=29)
First occurrence in the first cycle, %	
Yes	82.8%
No	17.2%
Median time to the first occurrence (range), days	20 (7-115)
Median duration (range), days	4 (1-14)
Leading to dose delay, %	19.6%
Leading to dose reduction, %	6.3%
Recovery, %	
within 7 days	89.7%
within 3 days	41.4%



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Conclusion

- **ESG401 shows promising antitumor activity in advanced breast cancer across three settings.**
  - Notably, it demonstrates significant efficacy in first-line TNBC patients.
  - This suggests that ADC drugs may be more effective when used earlier.

- **ESG401 has a manageable safety profile.**
  - Main TRAEs include leukopenia and neutropenia.
  - All Grade ≥3 leukopenia and neutropenia did not result in permanent treatment discontinuation.
  - No Grade ≥3 diarrhea, rash, or interstitial lung disease observed.

- **A phase 3 study of ESG401 monotherapy as first-line treatment for unresectable recurrent or metastatic TNBC is planned.**

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