Optimal Dose of Eribulin as 1st Line Treatment in Elderly Patients ≥ 70 Years with Advanced Breast Cancer: A Multicenter Phase II Trial [SAKK 25/14]

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Background

- In elderly patients (pts) with metastatic breast cancer (mBC), there is no generally accepted first line chemotherapy (CT) and only scarce data on any CT regimen (1).
- Eribulin mesylate (1.4 mg/m2)d1+8 in first line mBC achieved a clinical benefit rate (CBR; CR, PR or SD ≥ 6 months (mts)), of 26 - 52% (2). Less than 10% of pts in the registration-trial were ≥ 70 years (y)(3); dose reductions were frequent in the elderly.
- This trial (NCT02404506) aims to explore the efficacy of a reduced starting dose of eribulin as first-line treatment in elderly metastatic breast cancer pts.

Methods

- Eligibility: Female patients with:

a) locally advanced or metastatic HER2-neg, hormone receptor positive or negative adenocarcinoma of the breast
b) ≥ 70 years
c) adequate hematological values, hepatic function and renal function

- Treatment: Eribulin mesylate with reduced dose 1.1 mg/m2 d1+8 q3wk until progression
- Design: A single-arm 2-stage phase II trial
- Primary endpoint: Disease control (same definition as CBR)
- Secondary endpoints: objective response (OR), progression-free survival (PFS), overall survival (OS), patient reported neurotoxicity (FACT/GOG-Ntx)
- Hypothesis and sample size: Simon's optimal two-stage design to test H0 (CBR ≤ 35%) against H1 (CBR ≥ 50%) with a type-I error of 0.05 and power of 80% required 77pts

Results

From Aug 2015 to Feb 2019, 77 pts were accrued. All of them are evaluable for all endpoints.

Table 1. Baseline patients' characteristics

Variable	Value (N=77)
• Age at registration	
Median (Min–Max)	76 (70–89)
• WHO performance status	
0	33 (43%)
1	36 (47%)
2	8 (10%)
• Weight [kg]	
Median (Min–Max)	66.0 (47.9–114.0)
• Height [cm]	
Median (Min–Max)	160 (145–173)
• Body surface area (Mosteller) [m^2]	
Median (Min–Max)	1.7 (1.4–2.3)
• Previous anticancer therapies	67 (87%)
• Other clinically significant diseases	49 (64%)
• Liver metastases	35 (45%)
• Measurable disease	72 (94%)
• Hormone receptor positive	64 (83%)
• Bone metastases as only site of disease	2 (3%)

- Patients received a median number of 6 cycles (range: 1-24). Dose modifications were necessary in 35% of pts. Median dose per cycle was 2.1 mg/m2 (range: 1.1-2.3). In 9 pts, more than 15 cycles were given.
- Early dose reduction (i.e. during the first two cyles) occurred in 13 patients (17%). In 8 due to toxicity, 1 due to error and 4 by patients decision.
- Main reasons for treatment discontinuation were progressive disease (57%), patient refusal (14%), unacceptable toxicity (11%)

Table 2. Subgroup of patients with early* dose reduction (* during the first 2 cycles)

Variable	Early* dose reduction (N=13)	No early dose reduction (N=64)
Number of cycles >= 15	0 (0%)	9 (14%)
Liver metastases present	9 (69%)	26 (41%)

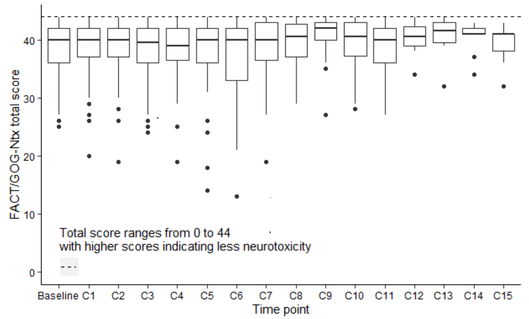
Table 3. Efficacy endpoints

Category	Variable	Value (N=77)
Primary endpoint	**CBR (90% CI)**	0.40 (0.31–0.50)
Secondary endpoints	**OR rate (95% CI)**	0.22 (0.13–0.33)
	Median PFS in month (95% CI)	5.4 (4.5–7.7)
	PFS events	63 (82%)
	Death	7
	Progression	56
	Median OS in month (95% CI)	16.1 (13.5–26.9)
	OS death reason	48 (62%)
	Other	1
	Progressive disease	40
	Unknown	7

- Forty-eight pts (62%) experienced at least G3 toxicity, including one patient with G5 (Death NOS, not clearly attributed to study drug)
- Neutropenia G3 was observed in 10%, G4 in 12% of pts. Two pts (3%) had febrile neutropenia
- Sensory neuropathy occurred in 23% (12% G1, 5% G2, 6% G3)
- Median patient-reported neurotoxicity scores remained stable for at least 15 cycles (Figure 1)

Acknowledgment: The trial was supported by Eisai, the Swiss State Secretariat for Education, Research and Innovation (SERI) Swiss Cancer Research Foundation (SCS) and Swiss Cancer League (SCL)

Figure 1. Patient-reported neurotoxicity



Conclusion

- We report the first prospective data on treatment with first line Eribulin mesylate in elderly pts.
- Reduced starting dose of 1.1 mg/m2 was safe and efficacy as expected, although the lower boundary of the 90% CI crossed the predefined threshold.
- A relevant subgroup of pts had prolonged disease control. None of the pts with early dose reduction had prolonged disease control, they received a median of 3 cycles.
- Long time treatment did not worsen patient-reported neurotoxicity.

Overall: Reduced starting dose in elderly may allow prolonged treatment and disease control without cumulative neurotoxicity. An early reduction of an already reduced starting dose was associated with early treatment failure.

References

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Poster presented at ESMO Virtual Congress 2020, Madrid

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