Sicurezza di Eribulina Mesilato concomitante a radioterapia nel carcinoma mammario metastatico: l'esperienza dell'Università di Firenze

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Metastatic breast cancer (MBC)

- Life expectancy of MBC patients has remarkably improved in the last 20 years
- A considerable number of systemic new therapies is now available
- ***Radiation therapy*** (RT) for painful bone metastases or ablative therapy in an oligometastatic scenario is therefore extremely frequent in the management of MBC patients

Treatments with survival end clinical benefit are greatly needed for women with heavily pretreated metastatic breast cancer

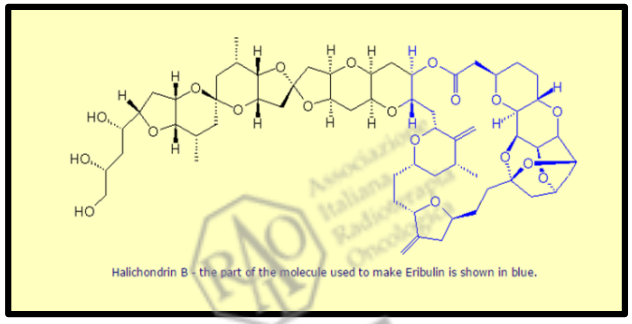
Eribulina

New agent approved for the treatment of metastatic breast cancer

Eribulin monotherapy versus treatment of physician's choice in patients with metastatic breast cancer (EMBRACE): a Phase 3 open-label randomised study.
Cortes J, O'Shaughnessy J, Loesch D et al. Lancet 377 (2011)

Phase III Open-Label Randomized Study of Eribulin Mesylate Versus Capecitabine in Patients With Locally Advanced or Metastatic Breast Cancer Previously Treated With an Anthracycline and a Taxane
Kaufman PA, Awada A, Twelves C et al. J. Clin. Oncol. 33(6)(2015)

Eribulina



- It is a structurally simplified synthetic analogue of halichondrin B;
- Was originally isolated from western Pacific sponge Halichondria okadai;

- **Inhibits the growth phase of microtubule** dynamics and sequesters tubulin into non productive aggregates blocking microtubule polymerization without affecting depolymerization: ***inducing irreversible mitotic blockade at G2-M phases and apoptosis***

Aim

This study evaluates, for the first time, the safety of Eribulin in metastatic breast cancer patients concomitantly treated with palliative radiotherapy.

Patients & materials

•17 patients for a total of 25 lesions underwent RT and concomitant Eribulin

Characteristic	Patients, n (%)
Age at BC diagnosis (years):	
– Median	52
– Range	26–65
Age at first metastases (years):	
– Median	58
– Range	26–69
ER- and/or PgR-positive status	16 (94.1)
Nuclear grade:	
– Grade 2	6 (35.3)
– Grade 3	11 (64.7)
Ki-67 proliferative index:	
– <15%	3 (17.6)
– ≥15%	14 (82.4)
HER2 status:	
– Positive	2 (11.7)
– Negative	15 (88.3)

BC: Breast cancer; ER: Estrogen receptor; PgR: Progesterone receptor.

- Patients mean age at time of BC diagnosis was 50 years (range: 26–65)
- **Mean *age* at time of initiation of eribulin therapy was 57 years** (range: 27–73)
- *Most patients had a hormonal positive BC and high proliferative index; a small proportion presented HER2-positive status.*

Patients & materials

Characteristic	Patients, n (%)
ECOG performance status:	
– 0	2 (12)
– 1	10 (59)
– 2	5 (29)
Prior chemotherapy line:	
– 2	7 (41)
– 3	2 (12)
– ≥4	8 (47)
Prior endocrine therapy line:	
– 0–1	10 (59)
– 2	4 (23)
– 3	3 (18)

- The majority of patients were **heavily pretreated**, with a prevalence of anthracycline- and taxane-based regimens
- **Patients had received a median of three lines of chemotherapy** (range: 2–7)

Patients & materials

Measures of ***pain score*** and ***analgesic consumption*** score were evaluated at each visit, using a patient-rated scoring system

- **PAIN** was analyzed using a **5-point scale**: 0 (none), 1 (mild), 2 (moderate), 3 (severe) or 4 (intolerable).

- **ANALGESIC USE** was scored on a **7-point scale**: 0 (none), 1 (mild analgesic or NSAID), 2 (mild analgesic and NSAID), 3 (moderate analgesic), 4 (opiates <40 mg morphine or equivalent, daily), 5 (opiates >40 mg, but <100 mg morphine or equivalent, daily), or 6 (opiates >100 mg morphine or equivalent, daily).

Results

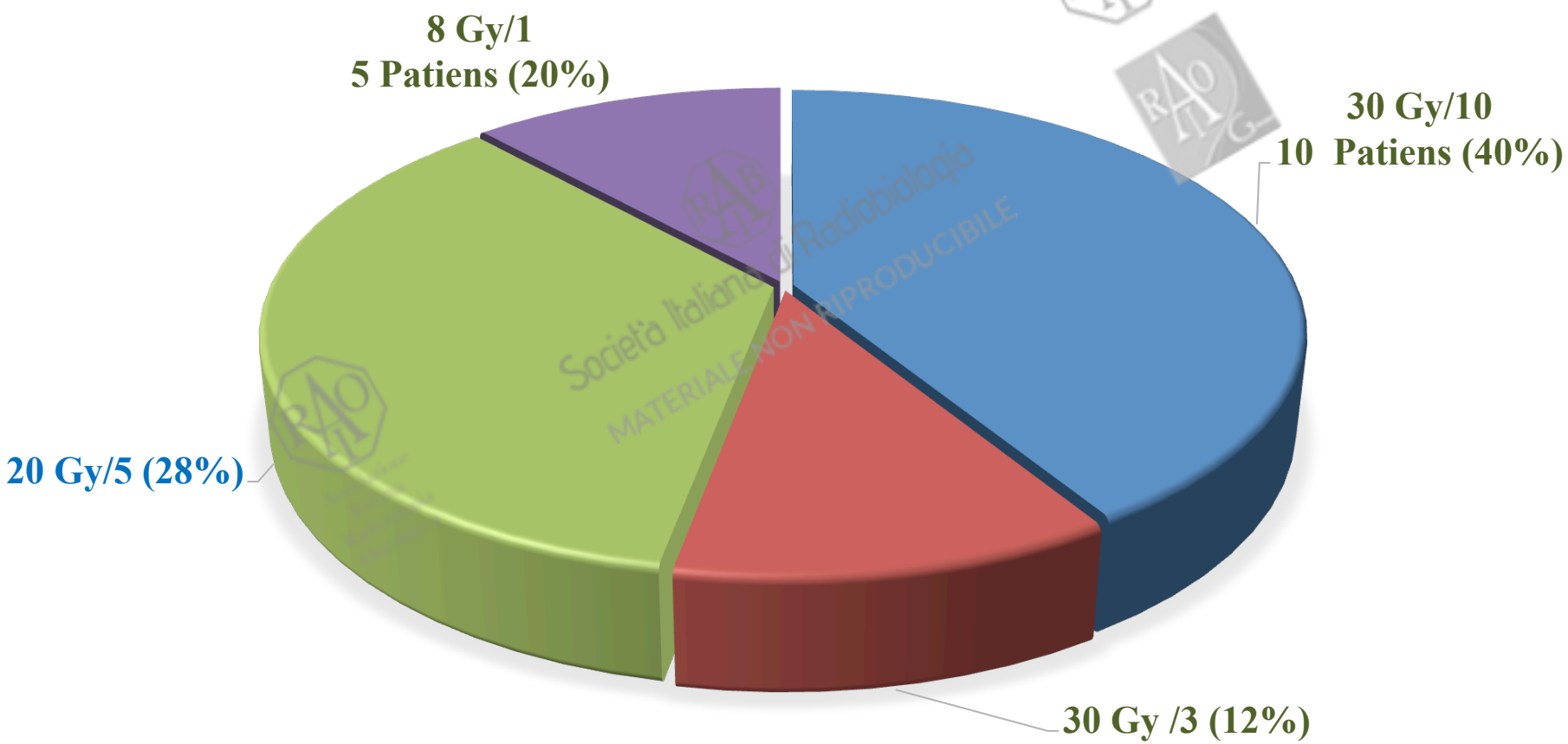
All patients received palliative bone RT or stereotactic treatment to extra-cranial lesions during eribulin treatment

Single lesion RT	N° of patients
Whole brain RT	1
Mediastinum RT	2
Stereotactic RT (1 lung, 1 bone and 1 liver lesion)	3
Bones	7
Total	**11**

Multiple bone sites RT	N° of patients
3 sites (vertebral bodies and pelvic bones)	2
2 sites (vertebral bodies and long bones)	4
Total	**6**

The concomitant administration of eribulin was started no later than 1 week from the beginning of the RT treatment

Results



Results

Eribulin Treatment:

- Patients received eribulin mesylate (1.4 mg/m2 intravenously) on days 1 and 8, of a 21-day cycle
- A median of **four cycles of eribulin** (range: 2–10) were administered.
- No suspension or delay in chemotherapy administration was necessary
- Six patients (35%) required a ***dose reduction*** due to hematological toxicity; ***none during RT***

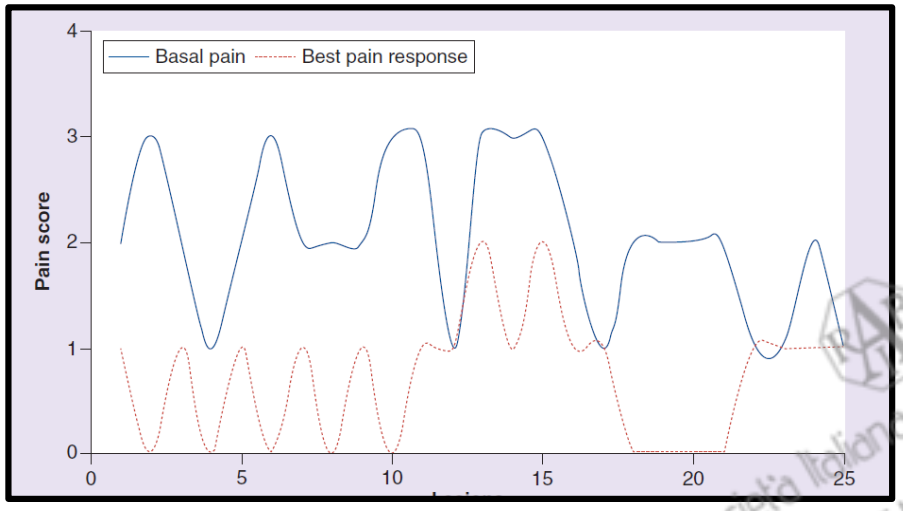
Results

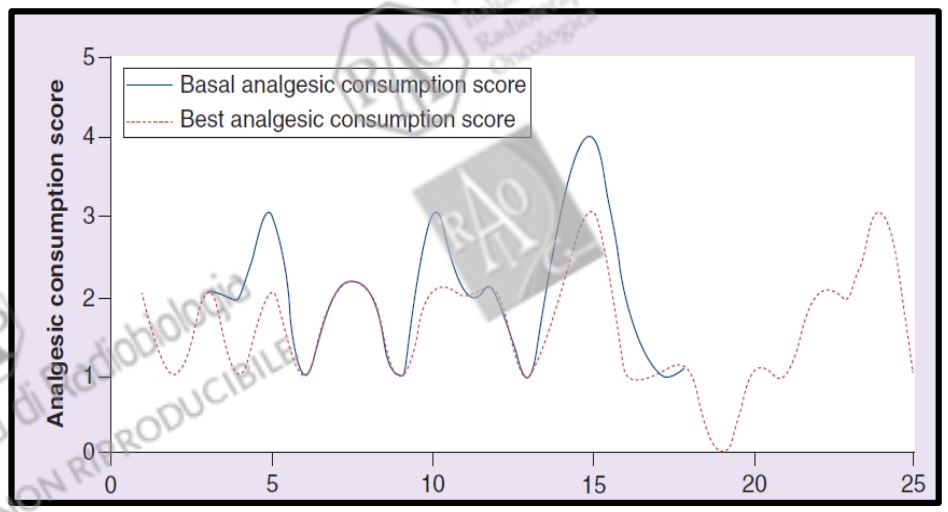
Advers Event: Hematologic	Grado I-II, n (%)	Grado III-Iva, n (%)	All Grade, n (%)
Anemia	5 (29,4)	1 (5,9)	**6 (35,3)**
Febrile Neutropenia	-	1 (5,9)	1 (5,9)
Leukopenia	2 (11,8)	4 (23,5)	6 (35,3)
Neutropenia	1 (5,9)	8 (47,1)	**9 (53)**

Advers Event: Gastrointestinal	Grado I-II, n (%)	Grado III-Iva, n (%)	All Grade, n (%)
Diarrhea	3 (17,7)	0	3 (17,7)
Nausea	7 (41,2)	0	7 (41,2)
Stomatitis	2 (11,8)	1 (5,9)	3 (17,7)
Vomiting	4 (23,5)	1 (5,9)	5 (29,4)

- ***Toxicity was manageable*** and in line with main published series.
- The most frequent hematological adverse events were neutropenia (53.1%) and anemia (35.4%)
- Less frequent was gastrointestinal disorders.

Results: Pain





Pain Score:
the mean BPS was **2** at baseline and **0.7** at the end of observation period.

Analgesic Consumption Score:
The mean ACS remained stable;
1.8 at baseline and 1.6 at the end of follow-up

Safety of eribulin mesylate and concomitant radiotherapy for metastatic breast cancer: a single-center experience. Meattini I. at Al. *Future Oncol*. 2016 May

Results: clinical outcome

At time of analysis, 16 patients have died due to disease progression; one patient was still on active treatment with everolimus and exemestane (median follow-up: 11 months; range:1–44).

The overall response rate was 29%
The clinical benefit rate was 59%

Conclusions

Eribulin is characterized by a manageable safety profile also when combined with palliative RT to bone metastases or ablative RT to visceral lesions.

Grazie per l'attenzione!