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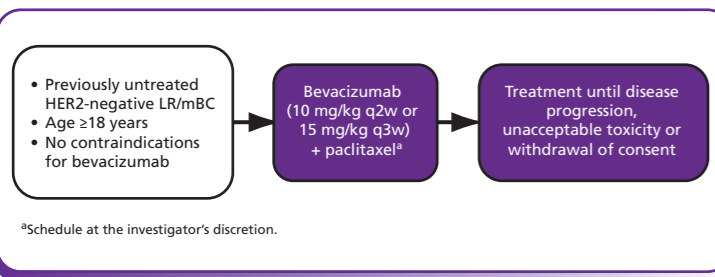
Background

- Triple-negative breast cancer (TNBC) presents a particular challenge for oncologists.
 - Data from prospective trials and subgroup analyses primarily in the first-line setting show median progression-free survival (PFS) of 2–6 months and median overall survival (OS) of approximately 1 year.^{1–6}
- Selection of the most appropriate treatment for these patients is hindered by the lack of data specifically in this setting.
 - There is no evidence to support use of one chemotherapy regimen over another.
 - The typical prognosis for patients with TNBC is poor, and therefore taxane therapy is a reasonable option to maximise the likelihood of response.
- In three randomised phase III trials, combining first-line bevacizumab with standard chemotherapy significantly improved PFS and response rate compared with chemotherapy alone in HER2-negative locally recurrent or metastatic breast cancer (LR/mBC).^{7–9}
 - Subpopulation analyses of the individual trials and a meta-analysis of all three trials suggest that the magnitude of benefit derived from bevacizumab in patients with TNBC is similar to that observed in the overall study population.^{10–12}
 - Median PFS was 6–10 months with first-line bevacizumab-containing therapy for TNBC in the randomised phase III trials and the ATHENA study.^{10,11,13}
- We report a subgroup analysis of patients with TNBC treated in a large German non-interventional study of first-line bevacizumab–paclitaxel combination therapy administered in the context of routine oncology practice.

Study design

- The study design is shown in Figure 1.
 - Endpoints were safety (adverse events [AEs], AEs of special interest, serious AEs) and efficacy (overall response rate, PFS, OS).
- Paclitaxel schedule, diagnostics and frequency of follow-up visits were at the discretion of the physician.
 - Data were collected for 1 year after the start of bevacizumab therapy, with one further follow-up for efficacy 1.5 years after the end of documented observation or discontinuation of bevacizumab, whichever occurred earlier.

Figure 1. Study design



Patient population

- At the time of data cut-off (31 January 2011) complete data from case report forms were available for 818 patients treated with bevacizumab–paclitaxel combination therapy.
 - Of these, 154 patients (19%) had TNBC.
 - The remaining 664 patients had positive or unknown oestrogen receptor, progesterone receptor and/or HER2 receptor status and were grouped together in the non-TNBC subgroup.
- Compared with the non-TNBC group, patients in the TNBC group were generally younger, had been more extensively treated with anthracycline and taxane therapy, had a shorter disease-free interval, were more likely to have lung metastases and had a higher tumour grade, which is consistent with the typical characteristics of patients with TNBC (Tables 1 and 2).

Table 1. Patient characteristics and treatment history

Characteristic	TNBC (n=154)	Non-TNBC (n=664)
Median age, years (range)	54 (26–79)	59 (28–87)
Age group, n (%)		
<40 years	14 (9)	35 (5)
40–49 years	38 (25)	123 (19)
50–59 years	47 (31)	188 (28)
60–69 years	33 (21)	207 (31)
≥70 years	22 (14)	111 (17)
ECOG PS, n (%)		
0	62 (40)	262 (39)
1	68 (44)	321 (48)
2	17 (11)	49 (7)
3	3 (2)	8 (1)
Missing	4 (3)	24 (4)
(Neo)adjuvant chemotherapy, n (%)	122 (79)	412 (62)
Anthracycline and taxane	55 (36)	128 (19)
Anthracycline, no taxane	58 (38)	199 (30)
Taxane, no anthracycline	2 (1)	12 (2)
Other/unknown	7 (5)	73 (11)

ECOG PS, Eastern Cooperative Oncology Group performance status.

Table 2. Disease characteristics

Characteristic, n (%)	TNBC (n=154)	Non-TNBC (n=664)
Disease-free interval <12 months ^a	58 (51)	74 (17)
Metastatic at first diagnosis	23 (15)	134 (20)
Metastatic sites at baseline		
≥3	45 (29)	223 (34)
Bone	52 (34)	388 (58)
Liver	36 (23)	312 (47)
Lung	71 (46)	209 (31)
CNS	6 (4)	11 (2)
Tumour grade		
1	0	19 (3)
2	43 (28)	357 (54)
3	101 (66)	213 (32)
Unknown/missing	10 (6)	75 (11)

^aPatients diagnosed with primary breast cancer; n=114 in the TNBC group, n=442 in the non-TNBC group.

Treatment exposure

- The mean (± SD) duration of bevacizumab therapy from the start of observation until the end of treatment (or the end of the observation period if earlier) was:
 - 6.8 (± 3.5) months in the TNBC group (range 1–16 months)
 - 7.6 (± 4.0) months in the non-TNBC group (range 0–36 months).
- The most common reason for discontinuation of bevacizumab was disease progression (47% of the TNBC group vs 42% of the non-TNBC group).
 - An additional 19% of the TNBC group discontinued because of death from breast cancer.
- Bevacizumab was continued beyond progression in:
 - 18 patients (12%) of the TNBC group
 - 74 patients (11%) of the non-TNBC group.

Efficacy

- At the time of data cut-off, PFS events had occurred in:
 - 118 patients (77%) in the TNBC group
 - 440 patients (66%) in the non-TNBC group.
- The overall response rate was 51% in patients with TNBC versus 65% in those with non-TNBC (Figure 2).
- Median PFS was:
 - 8.0 months in the TNBC group (Figure 3)
 - 10.1 months in the non-TNBC group.
- Median OS was:
 - 16.0 months in the TNBC group (events in 55%) (Figure 4)
 - 22.9 months in the non-TNBC group (events in 37%).

Figure 2. Best overall response

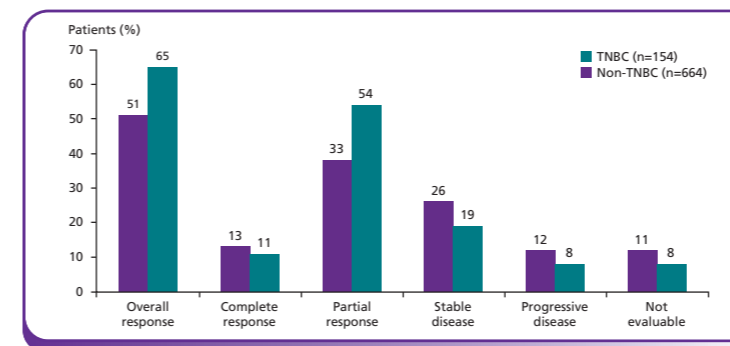


Figure 3. Progression-free survival in patients with TNBC (n=154)

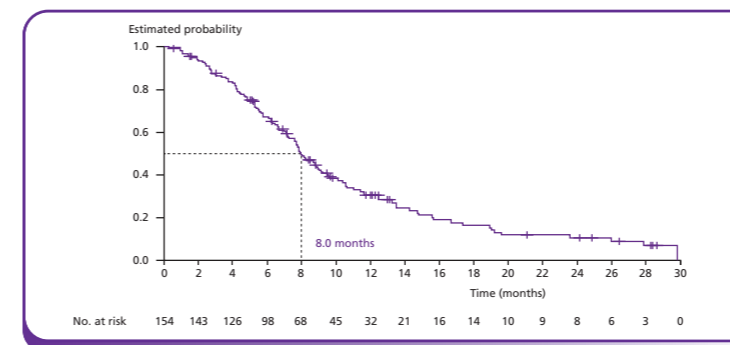
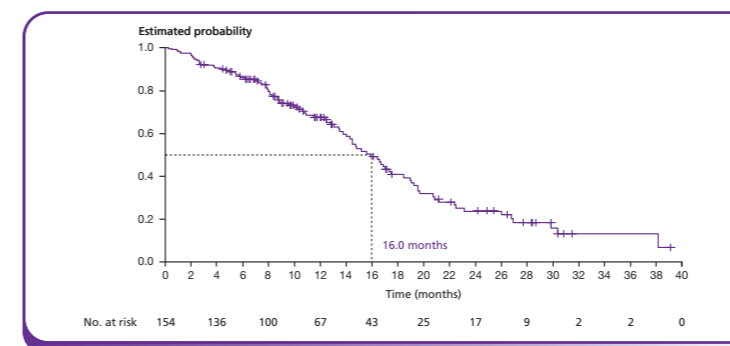


Figure 4. Overall survival in patients with TNBC (n=154)



Safety

- There were no major differences in the safety profile of bevacizumab–paclitaxel therapy between the two subgroups.
- The most common grade ≥3 clinical AEs in the TNBC group were pain, nausea and hypertension (Table 3).
- None of the patients with TNBC experienced grade 3/4 proteinuria, reversible posterior leucoencephalopathy syndrome or gastrointestinal perforation.
 - Two patients (1% with TNBC experienced arterial thromboembolic events; one of these was considered to be related to bevacizumab.
 - One patient in the TNBC group died from a haemorrhage. There were no other treatment-related deaths in the TNBC group.

Table 3. Most common (>1% of patients) grade ≥3 adverse events, irrespective of relationship to bevacizumab, in patients with TNBC (n=154)

Adverse event, n (%)	Grade	
	3	4
Leucopenia	14 (9)	0
Neutropenia	9 (6)	0
Anaemia	4 (3)	2 (1)
Pain	13 (8)	0
Nausea	5 (3)	0
Hypertension	5 (3)	2 (1)
Sensory neuropathy	3 (2)	0
Thrombosis/embolism	2 (1)	1 (<1)
Infection	1 (<1)	1 (<1)

Conclusions

- This exploratory subgroup analysis of a non-interventional study evaluating first-line bevacizumab–paclitaxel combination therapy in routine oncology practice suggests that the regimen is active in patients with TNBC.
- Bevacizumab combined with paclitaxel was well tolerated in the context of routine oncology practice.
- The efficacy results in TNBC are consistent with findings from subgroup analyses of phase III trials and the ATHENA study.^{10, 11, 13}
 - Median OS was 16.0 months in this analysis compared with 18.9 months in the meta-analysis of randomised trials and 18.3 months in ATHENA.
- Furthermore, the median PFS of 8.0 months and median OS of 16.0 months in patients with TNBC compare favourably with data reported for investigational agents in this setting.^{1–6}
- In the absence of randomised data defining the most appropriate treatment for patients with TNBC, it appears that bevacizumab in combination with paclitaxel is a reasonable and active treatment option.

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