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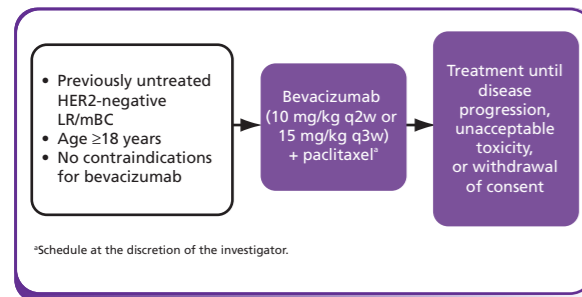
Background

- Triple-negative breast cancer (TNBC) presents a particular challenge for oncologists.
 - Data from a range of treatment lines, often retrospective, and from small numbers of patients, show median progression-free survival (PFS) of 2–6 months.¹⁻⁷
- 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 selection of one chemotherapy regimen over another. The prognosis for patients with TNBC is typically poor, and therefore taxane therapy is often administered to maximize the likelihood of response.
- Three randomized phase III trials have shown that combining first-line bevacizumab with a taxane or other standard chemotherapy significantly improves PFS and response rate compared with chemotherapy alone in HER2-negative locally recurrent or metastatic breast cancer (LR/mBC).⁸⁻¹⁰
 - Subpopulation analyses of the individual trials suggest that the magnitude of benefit derived from bevacizumab in patients with TNBC is similar to that observed in the overall study population.^{11,12}
 - Median PFS with first-line bevacizumab-containing therapy in the randomized phase III trials was 6–10 months.^{11,12}
 - Efficacy findings from the subpopulation of patients with TNBC treated in the ATHENA study were consistent with data from the randomized trials.¹³
- In Germany, a large, multicenter, non-interventional study has been conducted to provide further information on the safety and efficacy of first-line bevacizumab–paclitaxel combination therapy administered in the context of routine oncology practice.
 - We have previously reported findings from the entire study population¹⁴; here we present data from the subpopulation of patients with TNBC.

Study design

- The study design is depicted in Figure 1.
- Endpoints were safety and efficacy.
- Chemotherapy, diagnostics, and frequency of follow-up visits were at the discretion of the physician.
 - Data were collected and recorded for 1 year from 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



Results

Patient population

- At the time of data cut-off (December 31, 2009) case report forms were available for 567 patients treated with bevacizumab–paclitaxel combination therapy.
 - Of these, 115 patients had TNBC
 - The remaining 452 patients had positive or unknown estrogen receptor, progesterone receptor, and/or HER2 receptor status and were grouped together in the non-TNBC subgroup.
- Patient and disease characteristics and prior therapy at baseline are shown in Tables 1 and 2.
 - Patients in the TNBC group were generally younger, had a shorter disease-free interval, were more likely to have lung metastases, had been more extensively treated with anthracycline and taxane therapy, and had a higher tumor grade than those in the non-TNBC subgroup, consistent with the typical characteristics of patients with TNBC.

Table 1. Patient characteristics

Characteristic	TNBC (n=115)	Non-TNBC (n=452)
Median age, years (range)	53 (26–79)	59 (28–87)
Age group, n (%)		
<40 years	12 (10)	22 (5)
40–49 years	28 (24)	81 (18)
50–59 years	37 (32)	126 (28)
60–69 years	23 (20)	141 (31)
≥70 years	15 (13)	82 (18)
Premenopausal, n (%)	32 (28)	55 (12) ^a
ECOG PS, n (%) ^b		
0	43 (38)	173 (39)
1	52 (46)	221 (50)
2	14 (13)	37 (8)
3	3 (3)	7 (2)

^an=448. ^bn=112 in the TNBC group, n=438 in the non-TNBC group. May not total 100% due to rounding. ECOG PS, Eastern Cooperative Oncology Group performance status.

Table 2. Disease characteristics and treatment history

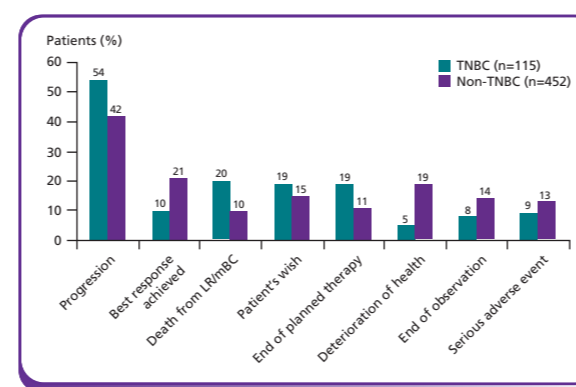
Characteristic	TNBC (n=115)	Non-TNBC (n=452)
Median time to relapse, years (range) ^a	1 (0–24)	1 (0–24)
<12 months, n (%)	49 (54)	56 (19)
Metastatic sites at baseline, n (%)		
Bone	38 (33)	263 (58)
Liver	27 (23)	223 (50)
Lung	54 (47)	140 (31)
CNS	4 (3)	8 (2)
Tumor grade, n (%) ^b		
1	0	14 (3)
2	30 (26)	240 (56)
3	79 (69)	147 (34)
Unknown	5 (4)	30 (7)
(Neoadjuvant) chemotherapy, n (%) ^c		
Anthracycline and taxane	43 (45)	81 (30)
Anthracycline, no taxane	44 (46)	130 (48)
Taxane, no anthracycline	1 (1)	6 (2)
Other/unknown	7 (7)	56 (21)

^aPatients diagnosed with primary breast cancer, n=91 in the TNBC group, n=299 in the non-TNBC group, n=114 in the TNBC group, n=431 in the non-TNBC group. ^bn=95 in the TNBC group, n=273 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:
 - 6.3 (± 3.3) months in the TNBC group
 - 7.1 (± 3.6) months in the non-TNBC group.
- Figure 2 shows the most common reasons for bevacizumab treatment discontinuation by subgroup.

Figure 2. Most common (>10%) reasons for bevacizumab treatment discontinuation



Efficacy

- At the time of data cut-off, PFS events had occurred in:
 - 70 patients (61%) in the TNBC group
 - 224 patients (50%) in the non-TNBC group.
- The overall response rate was 51% in patients with TNBC versus 62% in those with non-TNBC (Figure 3).
- Median PFS was:
 - 7.7 months in the TNBC group
 - 9.0 months in the non-TNBC group.

Figure 3. Best overall response

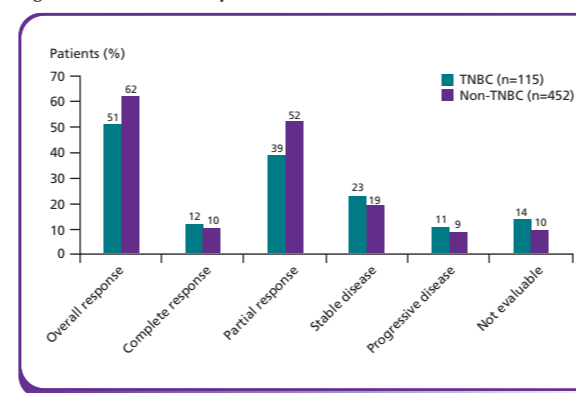
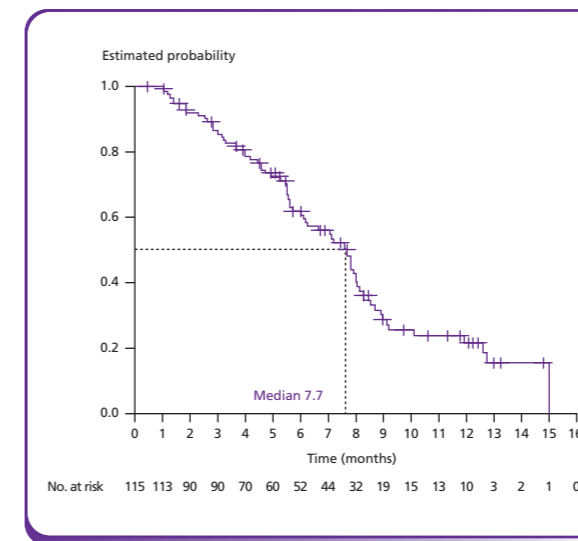


Figure 4. Progression-free survival in patients with TNBC (n=115)



Safety

- There were no major differences in the safety profile of bevacizumab–paclitaxel therapy between the two subgroups.
- Grade 3/4 adverse events in the TNBC group, irrespective of relationship to study treatment, are summarized in Table 3.
 - None of the patients with TNBC experienced grade 3/4 proteinuria, bleeding, gastrointestinal perforation, or arterial thromboembolic events.
- There were no treatment-related deaths in the TNBC subgroup.

Table 3. Grade ≥3 adverse events, irrespective of relationship to bevacizumab, in patients with TNBC (n=115)

Adverse event, n (%)	Grade	
	3	4
Pain	10 (8.7)	0
Hypertension	3 (2.6)	1 (0.9)
Cardiac dysfunction	1 (0.9)	0
Infection	0	1 (0.9)
Neurological effects	1 (0.9)	0
Hand-foot syndrome	1 (0.9)	0
Neuropathy	1 (0.9)	0

Conclusions

- This exploratory subgroup analysis of a non-interventional study evaluating 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 patients treated in the context of routine oncology practice.
- The efficacy results are consistent with observations from phase III trials and the ATHENA safety study.^{8-10,13}
- Furthermore, the median PFS of 7.7 months in the TNBC group compares favorably with data reported for investigational agents in TNBC.¹⁻⁵
- In the absence of randomized 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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