GAIN-2: Adjuvant Phase III Trial to Introduce dose-intensive (died) therapy with EnPC to Tailored dose-dense (dt) Therapy with dtEC-df for Patients with high-risk Early-Relapse Interventions: Results of the Second Safety Interim Analyses

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Background

• Sequential administration of single-agent therapies allows high doses and dose-intense schedules. Such intense dose-dense (idd) regimen (q2w) significantly increases hematological toxicity, but results in a very low event rate, thereby often being preferred in an idd regimen

• GAIN-2 compares efficacy and safety of a predefined idd regimen (EnPC) vs a dose-dense regimen where single doses are adjusted depending on individual hematological and non-hematological toxicities (dtEC-dt). A study recently compared the administration of trabumab s.c. to the abdominal wall vs high-dose chemotherapy.

• nab-Paclitaxel provides a better toxicity profile and higher efficacy compared to conventional taxanes and therefore might be preferred in an idd regimen

• High hematological toxicities were significantly increased in the idEC-p arm (Table 2). As for non-hematological side effects, alkylphosphatase (59 vs 40%), ALAT (69 vs 59%), peripheral sensory neuropathy (83 vs 60%), arthralgia (63 vs 49%), myalgia (48 vs 25%) and bone pain (25 vs 11%) and bone pain (25 vs 11%) were more common in the dtEC-dt arm. There was no difference between the treatment arms for the toxicities of special interest (cranial nerves, anaphylaxis, macula edema).

Results

• Between 09/2012 and 05/2015 a total of 1473 patients have been randomized to idEC-p (n=739) and dtEC-dt (n=734). Among those, 84 patients have been included in the tumourazm s.c. subcohort. No safety data are currently available for the subcohort. Baseline characteristics of patients in both arms are shown in Table 1.

• The second interim analysis showed no additional or unexpected safety signals in idEC-p or dtEC-dt arm and the study will be continued without changes.

Table 1: Hematological toxicities according to chemotherapy

| Adverse Event | Grade 1 | Grade 2 | Grade 3 | Grade 4 | P-value
|---------------|---------|---------|---------|---------|--------|
| Leukopenia     | any     | 447 (99) | 438 (88) | 988 (86) | .n.s.
| Neutropenia    | 3-4     | 425 (94) | 430 (92) | 828 (82) | .025
| Lymphopenia    | 3-4     | 473 (97) | 439 (93) | 872 (91) | .n.s.
| Thrombocytopenia| any     | 379 (81) | 347 (77) | 722 (80) | .043
| Febrile neutropenia | 3-4 | 54 (12.0) | 34 (7.6) | 88 (8.8) | .033
| Grade 1        | 3-4     | 473 (96) | 439 (93) | 872 (91) | .n.s.
| Grade 3        | 3-4     | 379 (81) | 347 (77) | 722 (80) | .043
| Grade 4        | 3-4     | 379 (81) | 347 (77) | 722 (80) | .043

Conclusions

The second interim analysis showed no additional or unexpected safety signals in idEC-p or dtEC-dt arm and the study will be continued without changes.

Reference