Efficacy and quality of life of NEPA as CINV-prophylaxis in highly or moderately emetogenic chemotherapy – interim results of a German prospective non-interventional study

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Background

The combination of 5-HT₃- and NK₁-receptor-antagonist (RA) and dexamethasone is recommended by current international anti-emesis guidelines for patients receiving highly emetogenic chemotherapy (HEC) and in certain patients receiving moderately emetogenic regimens (MEC)^{1,2,3}. Carboplatin is at the high end of the MEC category, with recent antiemetic guidelines recommending the use of an NK₁-RA, 5-HT₃-RA and dexamethasone in patients receiving carboplatin-based chemotherapy. The antiemetic guidelines of the Multinational Association of Supportive Care in Cancer (MASCC) and the European Society for Medical Oncology (ESMO)¹ recom-

mend the use of this triple combination for all carboplatin-based MEC regimens. The 2017 updated American Society of Clinical Oncology (ASCO) Clinical Practice Guideline on Antiemetics² recommends the three drug combination for adult patients who are treated with carboplatin area under the curve (AUC) ≥4 mg/mL per minute. In MEC-treated patients, the NK₁-RA-based three drug combination is also recommended by the National Comprehensive Cancer Network (NCCN) guidelines in patients with further high-risk factors, or if previous 5-HT₃-RA-dexamethasone treatment has failed.³ In patients receiving another platinum-analogue, oxaliplatin, higher no emesis-rates have been reported with an NK₁-RA-based antiemetic regimen compared to a two drug combination.⁴

NEPA (Akyneo®), a fixed combination capsule combining the long lasting NK₁-RA netupitant and the pharmacologically distinct 5-HT₃-RA palonosetron, has been approved for the prevention of acute and delayed chemotherapy-induced nausea and vomiting (CINV) in adult cancer patients receiving cisplatin-based HEC or MEC. Here we present an interim analysis of a real-life study of NEPA for CINV-prevention in patients receiving HEC, carboplatin-based MEC, and MEC.

1 Roila F et al. Ann Oncol 2016;27 (suppl5):v119-133
2 Hesketh PJ et al. J Clin Oncol 2017;35:3240-3261
3 NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Antiemesis. Version 3.2018 – June 11, 2018. https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Last accessed June 14, 2018
4 Nishimura J et al. Eur J Cancer 2015;51:1274-82

Methods

- Multi-center, prospective, open, non-interventional study (NIS)
- For CINV prevention NEPA is prescribed in accordance with the terms of the marketing authorisation (NEPA is orally administered 1 hour prior to the start of each chemotherapy cycle)
- The objective of the study is to assess the quality of life of adult patients receiving NEPA in the course of a one day or two days MEC or HEC
- Antiemetic prophylaxis with NEPA must be documented during 3 consecutive chemotherapy cycles per patient
- Primary endpoint: Quality of life as recorded by FLIE questionnaires on day 5 (6 for two day chemotherapies) of 3 consecutive chemotherapy cycles
- Secondary endpoints: efficacy of NEPA, use of rescue medication, safety data and AEs
- Efficacy ist documented by patient diaries (patients) and electronic case report forms (e-CRF) (physicians)

Interim analysis – Documentation:
Physicians Efficacy is documented by physicians using an e-CRF. Efficacy is assessed at the end of each of 3 consecutive cycles using 4 efficacy categories: Very good, good, satisfactory, poor.
Patients Patients used diaries for documenting the efficacy of the antiemetic prophylaxis with NEPA, the need for rescue medication and adverse events on days 1–5 (and up to day 6 for pts receiving a chemotherapy on two consecutive days) of 3 consecutive chemotherapy cycles. At the end of each of the 3 cycles, patients gave an overall assessment of efficacy using 4 efficacy categories: Very good, good, satisfactory, poor.

Patient characteristics

At the cut-off date 30.11.2017, 2 427 patients had been enrolled in the study. For the interim analysis 1 997 patients were evaluated that had been fully documented in the eCRF. Patients for whom a 5-HT₃ and/or NK₁-RA other than NEPA was documented as current treatment were excluded from efficacy analysis (n=95).

		November 2017 n=1 902
Female, n (%) Male, n (%)		1 620 (85.0 %) 282 (15.0 %)
Age (years)	Median Range	58 25–89
Tumor Type (n; %)	Breast	1 272 (65.3 %)
	Ovarian	130 (7.3 %)
	Colorectal	103 (5.8 %)
	Lung	90 (4.9 %)
	Cervical	46 (2.5 %)
	Stomach	40 (2.2 %)
	Pancreatic	37 (1.8 %)
	Non-Hodgkin Lymphom	28 (1.3 %)
ECOG-Status (%)	0	1 162 (61.1 %)
	1	621 (32.7 %)
	2	111 (5.8 %)
	3	8 (0.4 %)

86 % of the 1 185 patients receiving HEC had breast cancer. Of the 630 patients receiving MEC, 31 % had breast, 20 % ovarian, and 16 % colorectal cancer.

Regimens according to emetic risk*

* Roila F et al. Ann Oncol 2016; 27 (suppl 5):v119-v133 Hesketh PJ et al. J Clin Oncol 2017;35:3240-3261.

Results

Efficacy as recorded in patient diaries

Efficacy MEC reported by patients
n=401 (patients with analysed diary, eCRF entries)

Complete response**

No emesis#

No significant nausea**

No rescue medication#

* Only mild nausea as recorded in patient diaries. # patient diaries

Efficacy HEC reported by patients
n=896 (patients with analysed diary, eCRF entries)

Complete response**

No emesis#

No significant nausea**

No rescue medication#

* Only mild nausea as recorded in patient diaries. # patient diaries

Safety

To date (5.4.2018), 410 treatment-emergent adverse events (TEAEs) were documented. Among these, 81 grade 3 and 5 grade 4 events were reported. The most common treatment emergent adverse events were constipation and insomnia of mild-moderate intensity.

* Only TEAEs with more than 5 events are displayed. Chemotherapy-related events i.e. alopecia, fatigue, leukopenia, nausea, vomiting are not displayed.

Efficacy reported by physicians

Efficacy MEC reported by physicians n=630
Overall efficacy of antiemetic prophylaxis with NEPA during 3 consecutive cycles as assessed by physicians on a 4 point scale as recorded in eCRFs

Efficacy HEC reported by physicians n=1 185
Overall efficacy of antiemetic prophylaxis with NEPA during 3 consecutive cycles as assessed by physicians on a 4 point scale as recorded in eCRFs

Comparison of efficacy assessments by patients and physicians

Comparison MEC reported by patients and physicians
n=401 (patients with analysed diary, eCRF entries)

Comparison HEC reported by patients and physicians
n=896 (patients with analysed diary, eCRF entries)

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Conclusion

NEPA proved to be effective in the prevention of chemotherapy-induced nausea and vomiting induced by highly and moderately emetogenic chemotherapy. Complete response as reported in patient diaries was comparable between patients receiving MEC and patients receiving HEC. No-emesis-rates were almost identical between the MEC and HEC group. More than 93% of patients in both the MEC and the HEC-group reported no emesis on the 5 post-chemotherapy days in all 3 chemotherapy cycles. Moreover, the efficacy assessments of the antiemetic prophylaxis with NEPA were comparable between patients and physicians. Nausea is known to be more difficult to control.^{1,2} However, more than 75 % of MEC patients and ~ 62 % of HEC patients reported no significant nausea in this real-life study. NEPA was well tolerated with low-grade constipation being the most frequent treatment-related adverse event. The study is ongoing.

1 Hesketh PJ et al. J Clin Oncol 2017;35:3240-3261
2 Bošnjak S et al. Support Care Cancer 2017;25:1661-1671