

Feasibility of home delivery (HD) of Maintenance pemetrexed (PEM) therapy for advanced nonsquamous non small cell lung cancer (adv nsqNSCLC)

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ABSTRACT

Background: Some patients with adv nsqNSCLC may not need hospital-based chemotherapy. This study evaluated the feasibility and adherence to HD of maintenance PEM therapy in these patients. PEM is suitable for HD due to its favourable safety profile and ease of use (10-minute i.v. infusion).

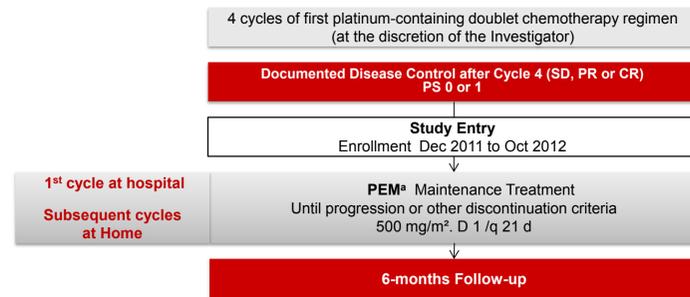
Methods: Exploratory, prospective, single-arm, Phase 2 study in adv nsqNSCLC patients, Eastern Cooperative Oncology Group (ECOG) performance status (PS) 0 or 1 without progression after 4 induction cycles of platinum doublet. The first cycle of PEM (500mg/m²) was hospital administered, further cycles as HD until progressive disease or discontinuation. Feasibility was assessed by the adherence rate to HD (probability of reversion to hospital administration or discontinuation due to HD) as primary endpoint, and by health related quality of life (HRQoL) (EQ-5D, lung cancer symptom scale [LCSS]), satisfaction with HD, Overall Survival (OS) and safety.

Results: 52 patients (UK/Sweden) had a median of 4 (range 1 to 19) maintenance PEM cycles. Adherence rate up to Cycle 6 was 98% (95% CI: 86.4%, 99.7%). All but 2 patients remained on HD. 1 patient discontinued after Cycle 1 (before first HD, patient decision) and 1 patient after Cycle 6 (investigator decision [non-compliance with oral dexamethasone]). 87% (33/38) patients preferred home treatment and in 90% (28/31) of cases, physicians were satisfied with distant patient management. During HD Cycles 2 to 4 mean change from baseline ranged from 3.0 to 7.7 for EQ-5D VAS and from -5.0 to -8.0 for LCSS average symptom burden index. The 6-month OS rate was 73% (95% CI: 58%, 83%). 1 patient had an HD related AE (device related infection Grade 2) and 1 patient died (possibly drug related atypical pneumonia).

Conclusions: HD of maintenance PEM therapy in adv nsqNSCLC was feasible, safe and preferred by patients, while maintaining HRQoL. Physicians were satisfied with distant patient management. Community-based clinical research requires specific consideration and resource allocation.

Study Design

- Multicenter, single-arm, open-label, phase 2 study, performed in the UK and Sweden.



*All patients received folic acid and vitamin B12 supplementation, and prophylactic dexamethasone according to the PEM label. Abbreviations: CR = complete response, d1 = Day 1, ECOG PS = Eastern Cooperative Oncology Group performance status, PEM = pemetrexed, PR = partial response, q21d = once every 21 days, SD = stable disease.

Statistical Methodology

- Kaplan-Meier methodology was used to estimate the rate of adherence to HD over time. Events were defined as reversion to hospital administration at any time after the beginning of study treatment. All patients who did not revert to hospital administration, but discontinue treatment, or discontinue the study for reasons other than HD strategy were censored on the last day of treatment.
- An adherence rate above 75%, when achieved at each cycle with at least 50% of patients remaining on study treatment, was considered sufficient to demonstrate the feasibility of HD.
- It was estimated that at the beginning of the Cycle 6, when more than 50% of patients were expected to have discontinued PEM treatment, a sample of 50 patients will be sufficient to observe the adherence rate of 86% with the lower limit of the 95% CI of 75%.
- HRQoL summaries are limited to Cycles 1 to 5 due to the low patient numbers (<20) for later cycles.

Questionnaire for Satisfaction with HD

- Individual questions prepared by the sponsor's health outcomes department [Lal R, 2013], concerning:
 - Physician satisfaction with distant management of the patient, completed at end of treatment.
 - Patient satisfaction with HD, a total of 16 questions evaluating:
 - hospital treatment experience
 - home treatment experience
 - home care nurses during HD treatment
 - preferences between hospital and home treatment
- Patient satisfaction questions were completed at the 30-day discontinuation visit and on the day of infusion for Cycle 4 in patients who received at least 4 maintenance cycles, the earlier of the 2 is reported here.

RESULTS

Demographics, Baseline and Disease Characteristics (N=52)

Parameter	
Sex	
Female/Male; n (%)	26/26 (50/50)
Age [years]	
Mean (STD)	64.3 (12.1)
Range	27.0 – 82.5
≥65 years; n (%)	28 (54)
ECOG Performance Status	
0: Fully active; n (%)	14 (27)
1: Restricted; n (%)	38 (73)
Most recent pathological diagnosis	
Adenocarcinoma, Lung; n (%)	48 (92)
Adenocarcinoma, Mucinous, NOS; n (%)	1 (2)
Adenocarcinoma, moderately differentiated, Lung; n (%)	1 (2)
Carcinoma, Non-small cell, Lung NOS; n (%)	2 (4)
Disease Stage	
Stage IIIA ^a ; n (%)	1 (2)
Stage IIIB; n (%)	3 (6)
Stage IV; n (%)	48 (92)

^a Patient enrolled because was considered by the physician as not eligible for curative treatment. Abbreviations: ECOG = Eastern Cooperative Oncology Group, NOS = not otherwise specified, STD = standard deviation.

Adherence to HD by Cycle (N=52)

- 50 patients adhered to HD; 2 patients met the HD failure criteria:
 - 1 patient due to patient decision: (Cycle 1 – before experiencing HD)
 - 1 patient due to physician decision: repeated non-compliance to oral dexamethasone (Cycle 6)

- Median number of treatment cycles (including Cycle 1): 4 (range 1 to 19).

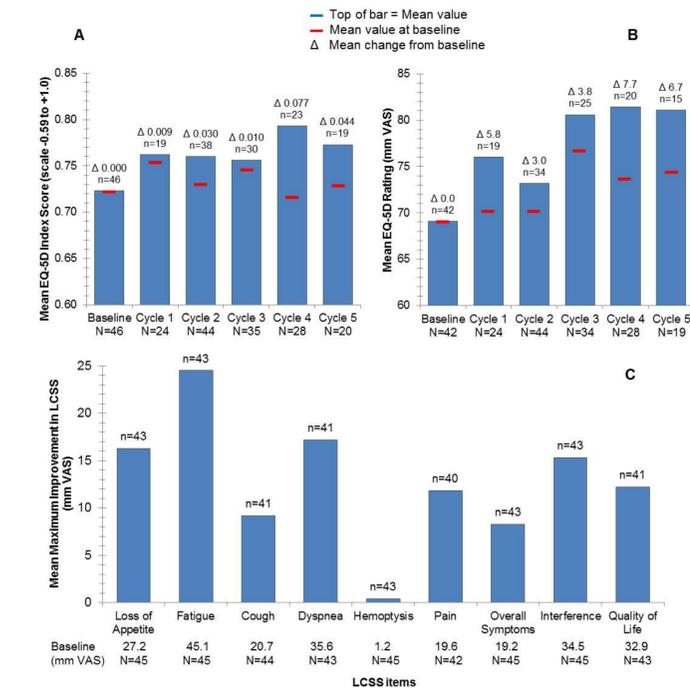
Setting	Cycle	Adherence rate % (95%CI)	Patients received cycle n (%)	Patients with discontinuation related to HD	Patients censored during cycle
Hospital	Cycle 1	100	52 (100)	1	6
	Cycle 2	98.0 (86.4, 99.7)	45 (86.5)	0	9
	Cycle 3	98.0 (86.4, 99.7)	36 (69.2)	0	7
	Cycle 4	98.0 (86.4, 99.7)	29 (55.8)	0	8
	Cycle 5	98.0 (86.4, 99.7)	21 (40.4)	0	7
	Cycle 6	98.0 (86.4, 99.7)	14 (26.9)	1	1
Home	Cycle 7	90.7 (61.7, 98.1)	12 (23.1)	0	0
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	Cycle 19	90.7 (61.7, 98.1)	1 (1.9)	0	1

Abbreviations: CI = confidence interval, HD = home delivery.

HRQoL during Maintenance Treatment with PEM

- Mean change from baseline of LCSS average symptom burden index ranged from -5.0 to -8.0 during HD Cycles 2 to 4.

A: EQ-5D mean index score. B: EQ-5D VAS mean rating. C: Mean maximum improvement from baseline (mm VAS) in LCSS items.



For graphs A and B, for the variable mean score/mean rating, all patients with post-baseline data in each cycle are included, with or without baseline data. The mean values at each cycle (top of bar) are based on all patients, whereas the mean values (red line) and changes from baseline (Δ) are based on patients with both baseline and post-baseline assessments. For graph C, the mean baseline LCSS VAS score (in mm) is shown below each LCSS item. Abbreviations: LCSS = Lung Cancer Symptom Scale, N = total number of patients, n = number of patients with data for change from baseline, VAS = visual analog scale.

Time to Treatment Failure and Overall Survival

- Median TTF: 3.0 months (95% CI: 2.3, 4.2)
- 6-month OS rate: 73% (95% CI: 58%, 83%)

Satisfaction with HD

Opinion of patients with respect to HD			
Advantages (>50%)	n (%)	Disadvantages	n (%)
No need to travel	37 (95)	Need to rely on 1 medical specialist	7 (21)
Personalized service	28 (72)	Lack of other patients support	5 (15)
Not having to wait for treatment	27 (69)	Safety concerns	4 (12)
More privacy	20 (51)	Extra burden for family/friends	1 (3)
Patients judgement on HD	n (%)	Physicians judgement on distant management	n (%)
Somewhat or very satisfied with HD	31 (91)	Very satisfied	20 (65)
Preferred HD	33 (87)	Somewhat satisfied	8 (26)
Preferred hospital administration	0	Somewhat dissatisfied	1 (3)
Were indifferent (HD vs hosp. adm.)	5 (13)	Very dissatisfied	2 (7)
Would recommend HD	37 (100)		

Resource Utilization

- Unplanned diagnostic procedures and visits to emergency facilities, general practitioners, or specialists were uncommon.
- Hospitalizations: 20 patients (39%) had at least 1 hospitalization with a median of total days in hospital of 6.5 (range: 2 to 34) days. 7 patients (13%) had 2 hospitalizations and 1 (2%) 3 hospitalizations. The main reasons for hospitalization were lower respiratory tract infection (3 patients, CTCAE Grade 2/3) and back pain (2 patients, CTCAE Grade 3).
- Blood transfusions: 13 patients (25%) received at least 1 transfusion of packed red blood cells (17/24 transfusions), whole blood (6/24) or platelets (1/24).

Safety

Related TEAES by CTCAE Grade and Preferred Term (all Grade 3/4 CTCAEs) (N=52)

Preferred Term	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)
At least 1 event (any term)	7 (13)	24 (46)	9 (17)	5 (10)
Hematological				
Neutropenia	1 (2)	-	-	3 (6)
Thrombocytopenia	-	1 (2)	-	2 (4)
Anemia	2 (4)	7 (13)	3 (6)	1 (2)
Non-Hematological				
Dyspnea	1 (2)	2 (4)	-	1 (2)
Pulmonary fibrosis	-	-	-	1 (2)
Sepsis	-	-	-	1 (2)
Fatigue	3 (6)	10 (19)	6 (12)	-
Nausea	9 (17)	4 (8)	1 (2)	-
Lower respiratory tract infection	-	1 (2)	1 (2)	-

- The most frequent (occurring >5% of patients) additional Grade 1/2 AEs were: Lethargy, Decreased appetite, Blood creatinine, Vomiting, Diarrhoea, Lacrimation increased, Constipation, Joint swelling, Dizziness, Rash, Stomatitis, and Dysgeusia.
- 1 patient died due to a possibly drug related atypical pneumonia.

DISCUSSION AND CONCLUSIONS

- HD of PEM was considered feasible, with an adherence rate >75% (98%, CI: 86.4, 99.7) at Cycle 4 (>50% patients), and at Cycle 5 and 6.
- The HRQoL was maintained, with mean EQ-5D and LCSS scores of patients not deteriorating throughout HD cycles.
- 87% of the patients preferred HD over hospital treatment.
- Physicians were "very satisfied" or "somewhat satisfied" with distant patient management for 90% (28/31) of the patients.
- The safety profile was consistent with PEM single agent in maintenance phase 3 trials.
- Limitation: the median OS could not be reliably estimated due to the small sample size and short duration of the study.
- HD of PEM as maintenance treatment in adv nsqNSCLC was feasible, safe, and preferred by patients, while maintaining HRQoL. Physicians were satisfied with distant patient management.

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