

A multicenter, randomized phase II trial of vinflunine and gemcitabine versus carboplatin and gemcitabine as first line treatment in patients with metastatic urothelial carcinoma unfit for cisplatin based chemotherapy due to impaired renal function – VINGEM.

Holmsten K¹, Jensen NV², Sonne Mouritsen L³, Agerbæk M⁴, Kempel MM⁵, Trepkas R⁶, Lahdenperä O⁷, Öfverholm E⁸, Mellnert C⁹, Cwikiel M⁹, Jonsson E¹⁰, Nilsson C¹¹, Shah C-H¹, Johansson H¹, Brandberg Y¹, von der Maase H¹², Pappot H¹², Ullén A¹

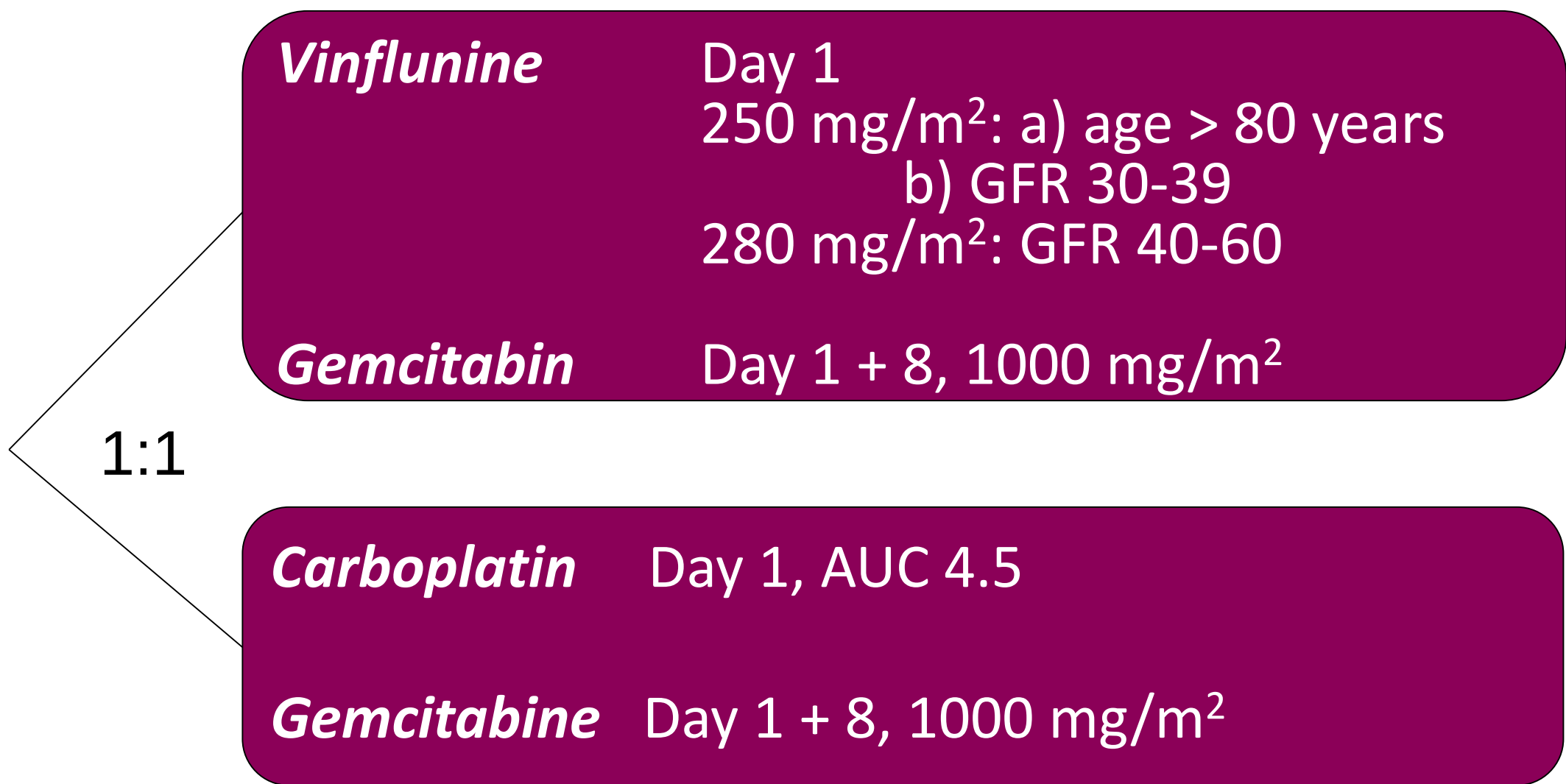
¹Karolinska Universitetssjukhuset, Stockholm, Sweden, ²Odense Universitetshospital, Odense, Denmark, ³Herlev Hospital, Herlev, Denmark, ⁴Aarhus Sygehus, Aarhus, Denmark, ⁵Aalborg Universitetshospital, Aalborg, Denmark, ⁶Næstved Sygehus, Næstved, Denmark, ⁷Åbo Universitetscentralsjukhus, Åbo, Finland, ⁸Sahlgrenska Universitetssjukhuset, Göteborg, Sweden, ⁹Skånes Universitetssjukhus, Malmö/Lund, Sweden, ¹⁰Norrlands Universitetssjukhus, Umeå, Sweden, ¹¹Västmanlands Sjukhus, Västerås, Sweden, ¹²Rigshospitalet, Copenhagen, Denmark.

Introduction and objectives: Standard first line treatment for patients with metastatic urothelial carcinoma (mUC) unfit for cisplatin is carboplatin containing combination-chemotherapy and immunotherapy with anti-PDL1/PD-1 MAbs. The median overall survival is limited to 8-10 months for chemotherapy and up to 15.9 months for immunotherapy. The development of more effective treatments remains an unmet medical need. Vinflunine has proven efficacy in mUC in second line treatment. The combination of vinflunine and gemcitabine has not yet been evaluated in mUC. The aim of this trial is to compare the efficacy, safety and quality of life of vinflunine and gemcitabine versus carboplatin and gemcitabine as first line treatment in patients with mUC unfit for cisplatin, due to renal impairment.

Material and methods: VINGEM is a randomized, multicenter phase II trial, performed at 12 Nordic centers associated to Nordic Urothelial Cancer Oncology Group (NUCOG). The main inclusion criteria are: metastatic mUC, first line palliative treatment, creatinine clearance 30-60 ml/min and ECOG PS 0-1. Patients in the experimental arm receive vinflunine 250 mg/m² or 280 mg/m² (depending on age and GFR) on day 1 and gemcitabine 1 000 mg/m² on day 1 and 8. Patients in the control arm receive carboplatin AUC 4.5 on day 1 and gemcitabine 1 000 mg/m² on day 1 and 8. In both arms, treatment continues every 21 days until disease progression, unacceptable toxicity or if patient wishes to stop treatment. The primary endpoint is progression-free survival (PFS). Secondary endpoints are overall response-rate (ORR), overall survival (OS), disease control rate (DCR), safety and Quality of Life (QoL). The study is designed as a non-definitive randomized phase II screening trial, designed to detect an increase in median PFS from 5 months to 9 months using a significance level of 10% and a power of 80%. To be able to detect a difference of this magnitude the study will include 60 patients.



VINGEM
A Nordic Urothelial Cancer Oncology Group Study



Center	2014	2015	2016	2017
Aalborg	1		1	
Aarhus		1		2
Herlev		3	1	2
Odense		4	2	7
Rigshospitalet		1	1	2
Göteborg			1	
Skåne		3	2	
Stockholm		1	3	5
Umeå	3		3	
Västerås		1	2	
Åbo			1	
Total/year	4	14	17	18
Total	4	18	35	53

Results: To date, 53 patients have been randomized. Regular safety assessment show so far expected and manageable side-effects. No SUSARs have been reported.

Conclusion: This is the first randomized clinical trial investigating the combination of vinflunine and gemcitabine in patients with mUC unfit for cisplatin based chemotherapy in first line treatment. The accrual rate is favorable and it is estimated that all 60 patients have been included by Q4-2017. ClinicalTrials.gov ID: NCT02665039.



Nordic Urothelial Cancer Oncology Group