

Vinflunine as second line chemotherapy for patients with metastatic urothelial cancer - A Nordic multi-center retrospective study

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Introduction and objectives: In 2009 Vinflunine (VFL) was introduced as the first, and so far only approved second line treatment after platinum failure for patients with metastatic transitional cell carcinoma of the urothelium (TCCU). The aims of this study were to analyze patient characteristics, treatment patterns, toxicity and efficacy of VFL-treatment at three Nordic centers associated to Nordic Urothelial Cancer Oncology Group (NUCOG).

Methods: Medical records based, retrospective analysis of patients with metastatic TCCU treated with VFL following to platinum failure.

Results: All patients (n=100) treated with VFL between 2009 and 2013 at three Nordic centers have been included in the analysis. Patient characteristics (sex, age, Hb, GFR), previous treatment and location of metastatic lesions are presented in Table 1. ECOG PS was 0 in 30%, 1 in 50% and 2 in 20% of the patients.

The median number of VFL cycles were 3 (range 1-28) and the most common starting dose was 280 mg/m² (46%). 12 % of the patients stopped VFL treatment due to toxicity. The most frequent grade 3 or 4 toxicities were: anemia (33%), neutropenia (23%), febrile neutropenia (13%), fatigue (36%), abdominal pain (12%) and constipation (22%).

Efficacy data show an overall response rate (ORR) of 27% (1 patient with complete response (CR)), stable disease (SD) as best response in 32% and progressive disease (PD) in 41% of the patients (Figure 5). The median progression free survival (mPFS) and median overall survival (mOS) were 3.3 months (95% CI, 0.5-34.3) and 6.4 months (95% CI, 0.3-39.2), respectively (Figure 1 and 2).

The group of patients with ECOG PS 2 (n=20) received in median 2 cycles of VFL (1-21) and showed no responses (41% SD, 59% PD). Moreover, these patients demonstrated a mOS of 3.9 months (95% CI, 1.2-16.1) compared to a mOS of 7.2 months (95% CI, 0.3-39.2) for patients with ECOG PS 0/1. Interestingly, 6 patients with ECOG PS 2 showed an OS of 6 months or more and 9 patients with ECOG PS 0/1 had an overall survival that exceeded 18 months.

ECOG PS was the main prognostic factor for OS (p=0.001) in this material (Figure 3). Presence of liver metastasis and Hb < 10 g/dL showed a trend to associate with OS but these factors were not significant (Figure 4). Furthermore, analyses are ongoing to evaluate efficacy parameters in relation to the number and type of previous given chemotherapy as first line treatment.

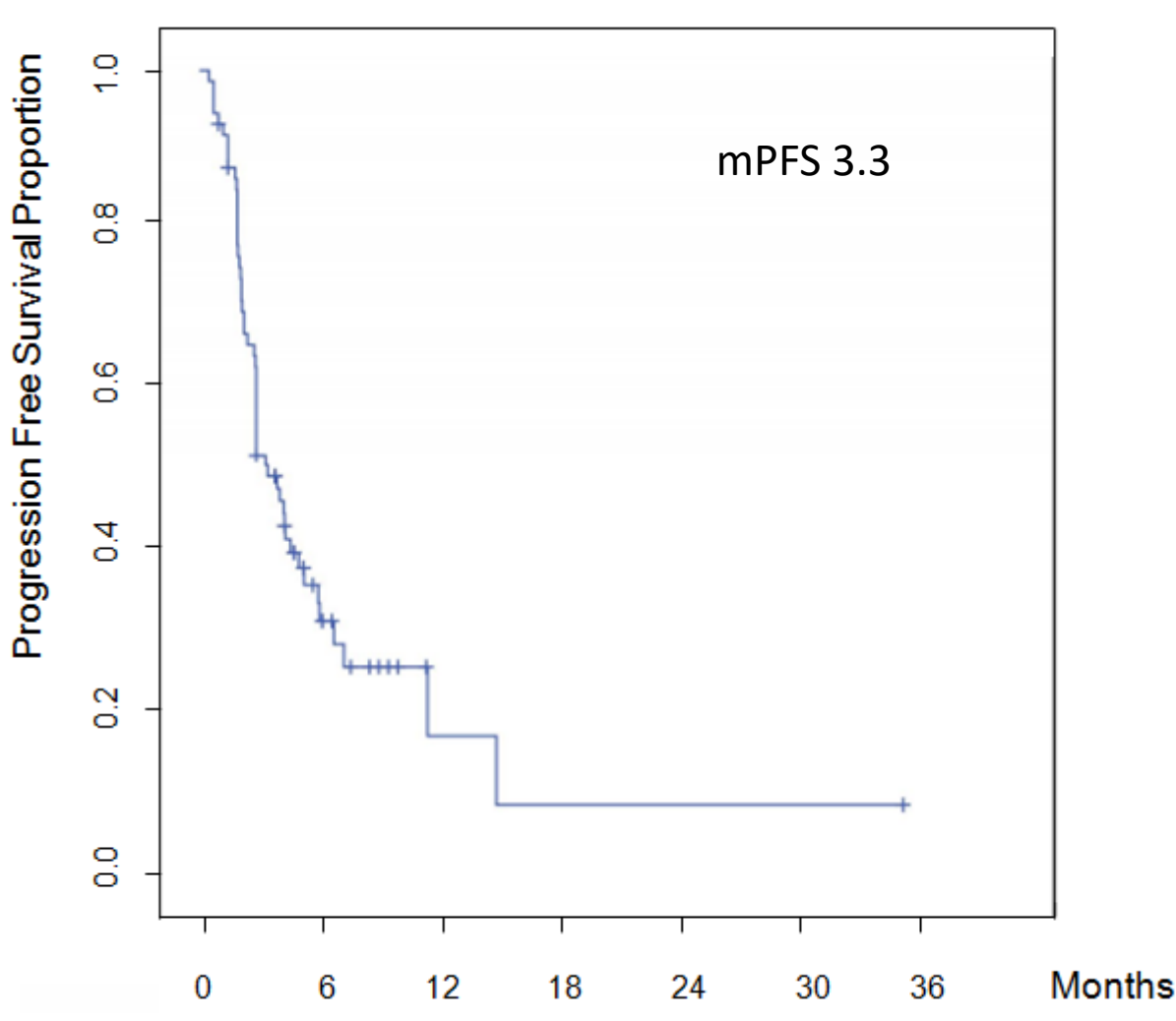


Figure 1. Progression-free survival, PFS

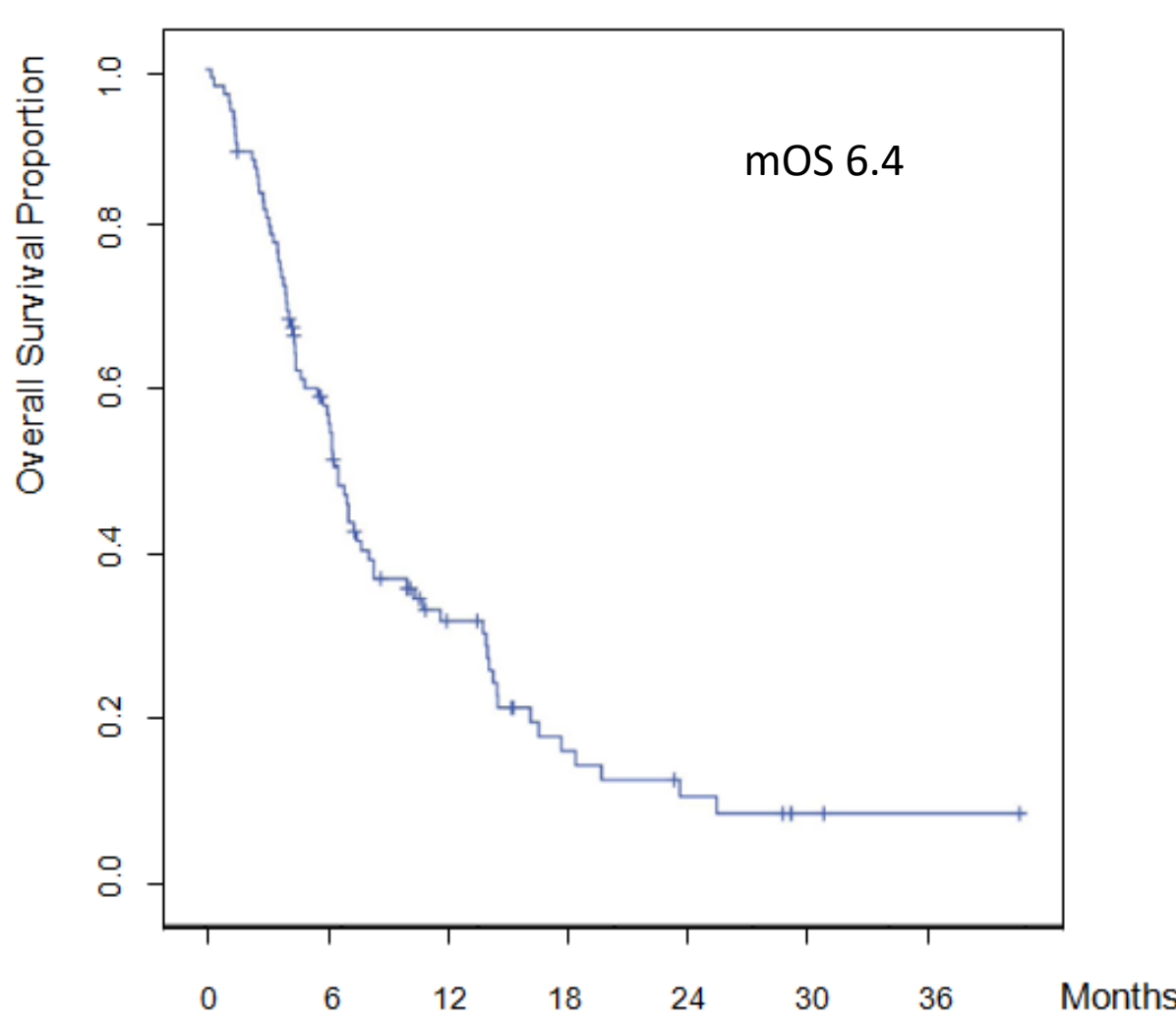


Figure 2. Overall survival, OS

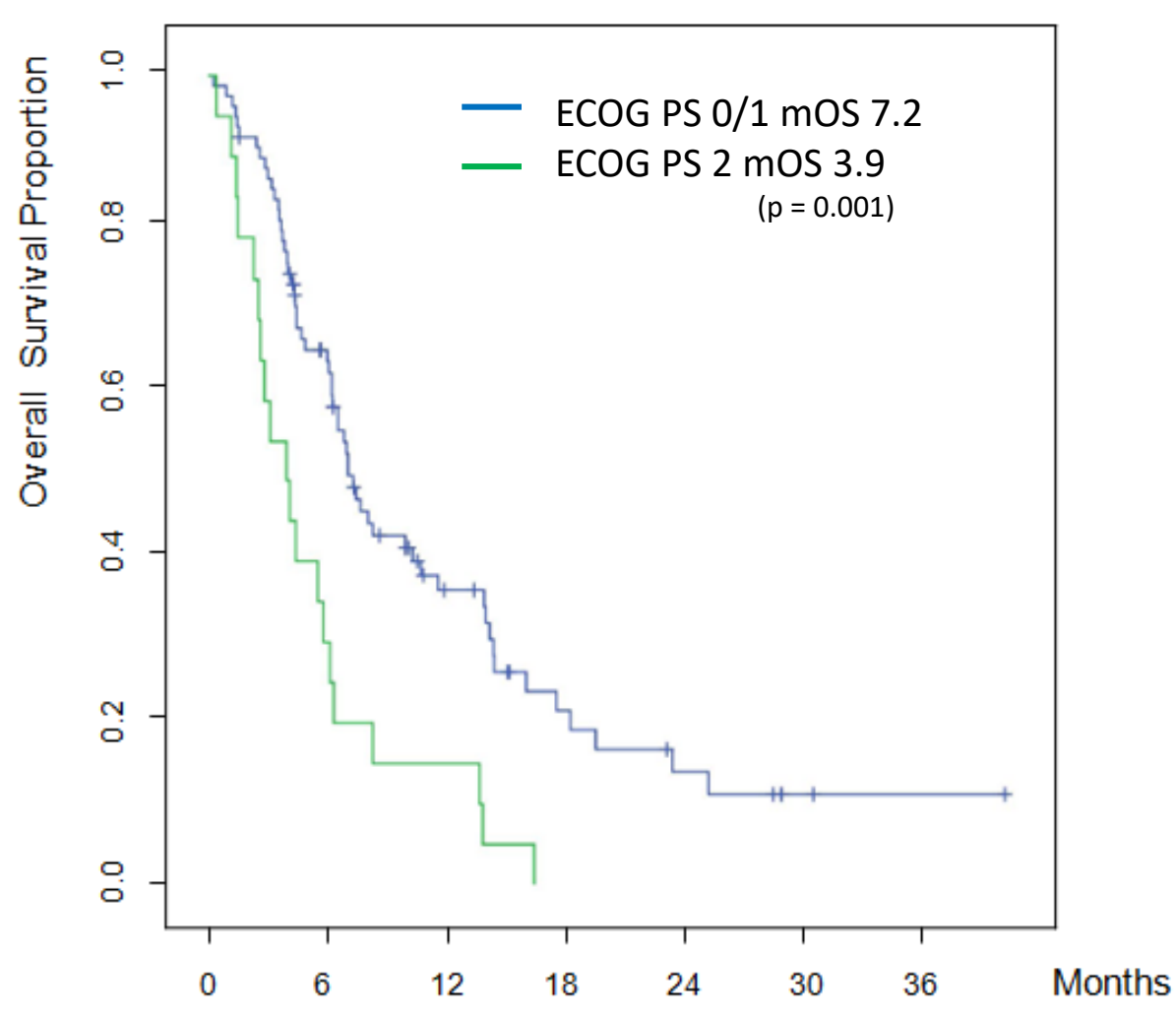


Figure 3. OS as a function of ECOG PS 0/1 vs 2

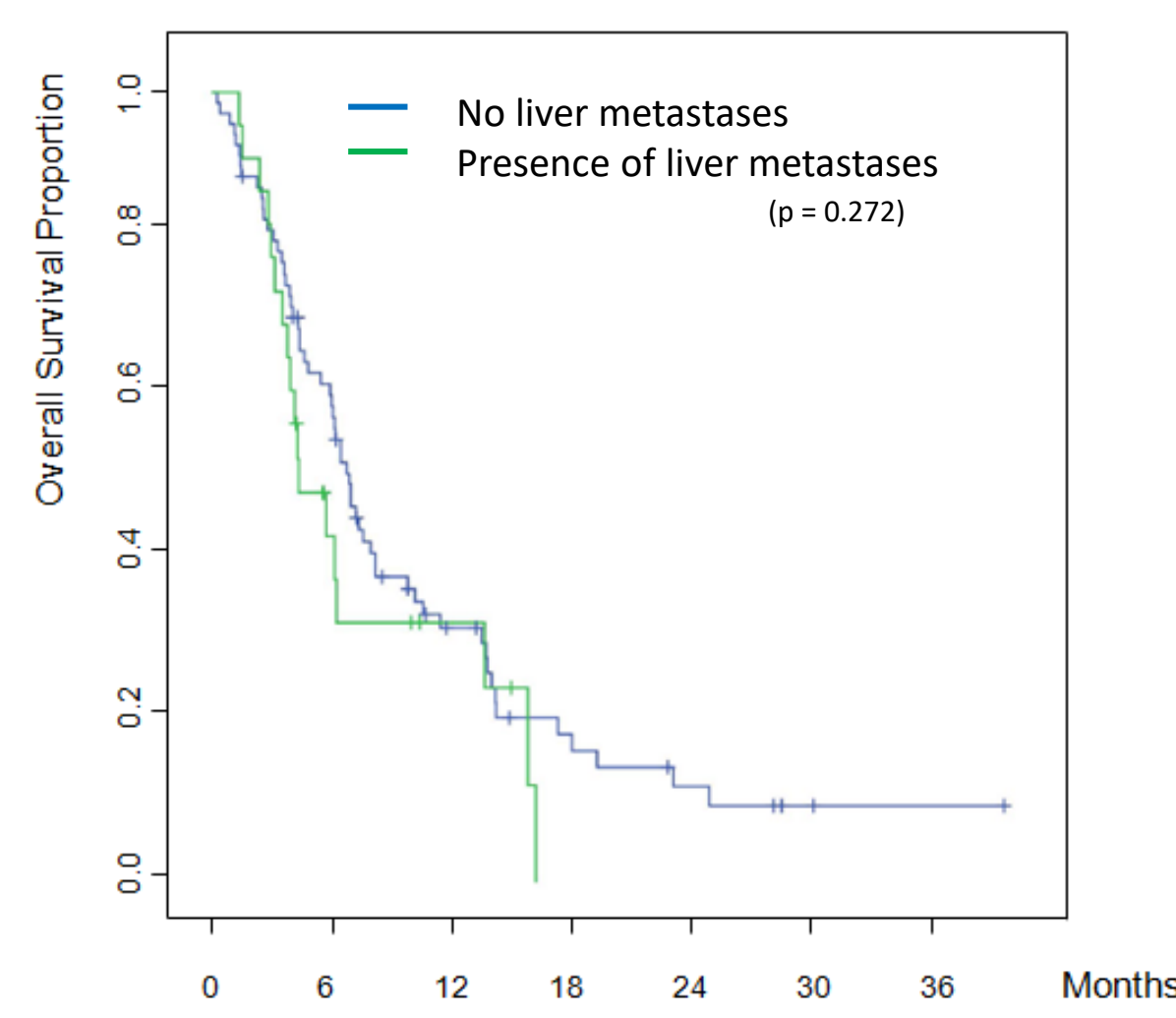


Figure 4. OS as a function of liver metastases

Patient characteristics	%
Sex - Male	72
Female	28
Age (years) - Median	68
Range	45-81
Hb - ≥ 10 g/dL	61
< 10 g/dL	39
GFR (ml/min) - Median	58
Range	21-124
Metastatic location	
Lymph nodes	65
Lung	47
Liver	25
Bone	18
Other	17
Primary therapy	
Primary surgery or RT	52
Peri-operative chemotherapy	27
1 st line palliative chemotherapy	
Median nr of cycles	6
Range	0-20
≥ 6 cycles	62
Gem/Cis	70
Gem/Carbo + Gem alone	19
No pall chemo before VFL	11

Table 1. Patient characteristics

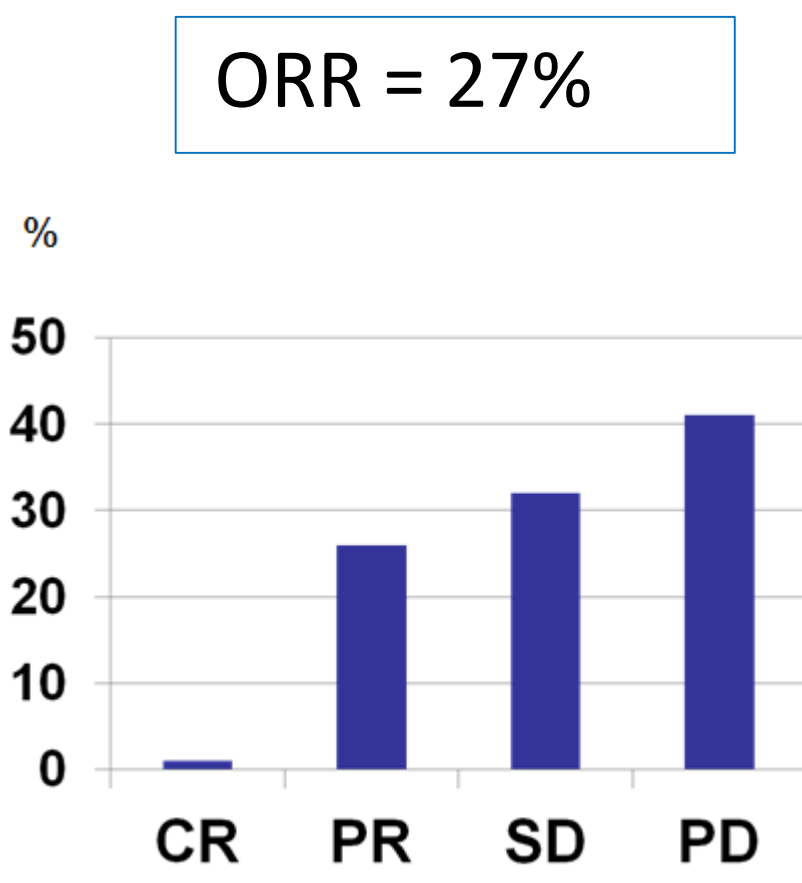
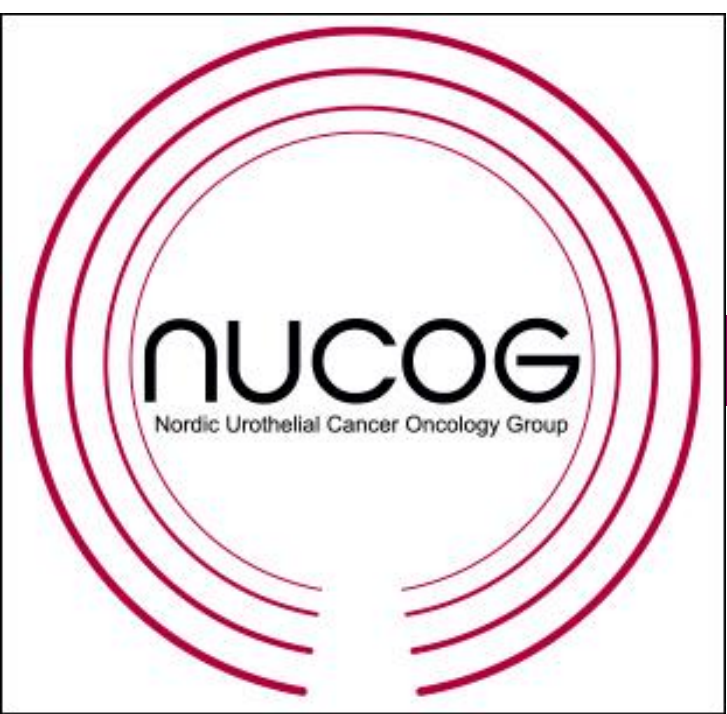


Figure 5. Response Rate

Conclusion: Our data confirm that VFL is an active agent for second line treatment in an unselected clinical routine cohort of patients with metastatic TCCU. ECOG PS was the main prognostic factor for OS (p=0.001) and in general, survival parameters were similar to previously reported phase II and phase III data for VFL. For patients with ECOG PS 2, which have not been reported previously, VFL treatment was tolerable, the mOS significantly shorter but some patients had a long phase with stable disease.

Interestingly, we observe significant inter-individual differences in treatment efficacy which highlight the importance of proper patient selection and the need for reliable prognostic factors and predictive biomarkers for second line VFL treatment of metastatic TCCU.



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