

Outcome of patients with advanced endometrial and cervical cancer treated in a phase 1 unit

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Introduction

- Patients with advanced endometrial and cervical cancers have limited therapeutic options and the prognosis is poor
- Median overall survival following 1st line therapy for advanced disease is.....
- Early phase trials may be a suitable option for patients with good performance status
- Increasingly, molecular characterisation guides pt selection for early phase trials
- We sought to determine the outcome of endometrial and cervical cancer patients treated in a phase 1 unit and examined the role of molecular selection to inform therapeutic decision making

Methods

- Medical records of all patients with an endometrial, cervical, vaginal or vulva malignancy treated within an early phase trial between 2010 and 2016 were reviewed
- Data comprising patient and tumor characteristics, prior treatment, trial therapy and outcome were analysed
- Next Generation Sequencing (NGS) profiling was performed, where available using a 22 gene amplicon-based panel (Life Technologies Colon & Lung V2)
- Detected variants are reviewed at a local genomics review board to assess potential actionability prior to considering therapy

Results

- 43 patients were identified with a diagnosis of endometrial cancer (EC, 23) or cervical/vulva cancer (CVC, 20) and treated on 46 allocated trials
- Median age 59 years (range 20-80)
- Median prior therapies 1 (0-3)
- 21 patients (46%) ≥ 2 prior therapies for advanced disease

Histological subtype	N
Endometrial High grade serous	8
Clear cell	1
Carcinosarcoma	4
Endometrioid	8
Other	5

Histological subtype	N
Cervix/Vulva Squamous	13
Adenocarcinoma	5
Clear cell	2
Neuroendocrine	1

Next Generation Sequencing (NGS)

- NGS was successfully performed in 20 patients (47%)
- 90% (18/20) of patients had a detected variant in ≥ 1 gene

NGS

- An actionable mutation identified in 55% (11/20), including KRAS (5 patients), PIK3CA (6 patients) and EGFR, PTEN and AKT (1 each)

Phase 1 Trial Enrolment

- Pts were allocated in order of priority as follows:
 - (1) a trial selected on the basis of NGS ('genomic', 15%),
 - (2) a 'tumour specific' cohort within an early phase trial (59%)
 - (3) a 'generic' study (26%)
- Genotype directed trials included PI3K, FGFR, mTOR and MEK inhibitor studies
- Trials with tumour specific cohorts included novel chemotherapy agents, antibody-drug conjugates and single and combination immunotherapy studies
- Generic studies included novel chemotherapy, ATR inhibitor and vascular disrupting agents

Outcome: Response Rates

- 41 patients (89%) are evaluable for response
- The overall response rate (ORR, complete and partial responses as defined by RECIST) was 22% with a clinical benefit (ORR and stable disease) rate of 63%

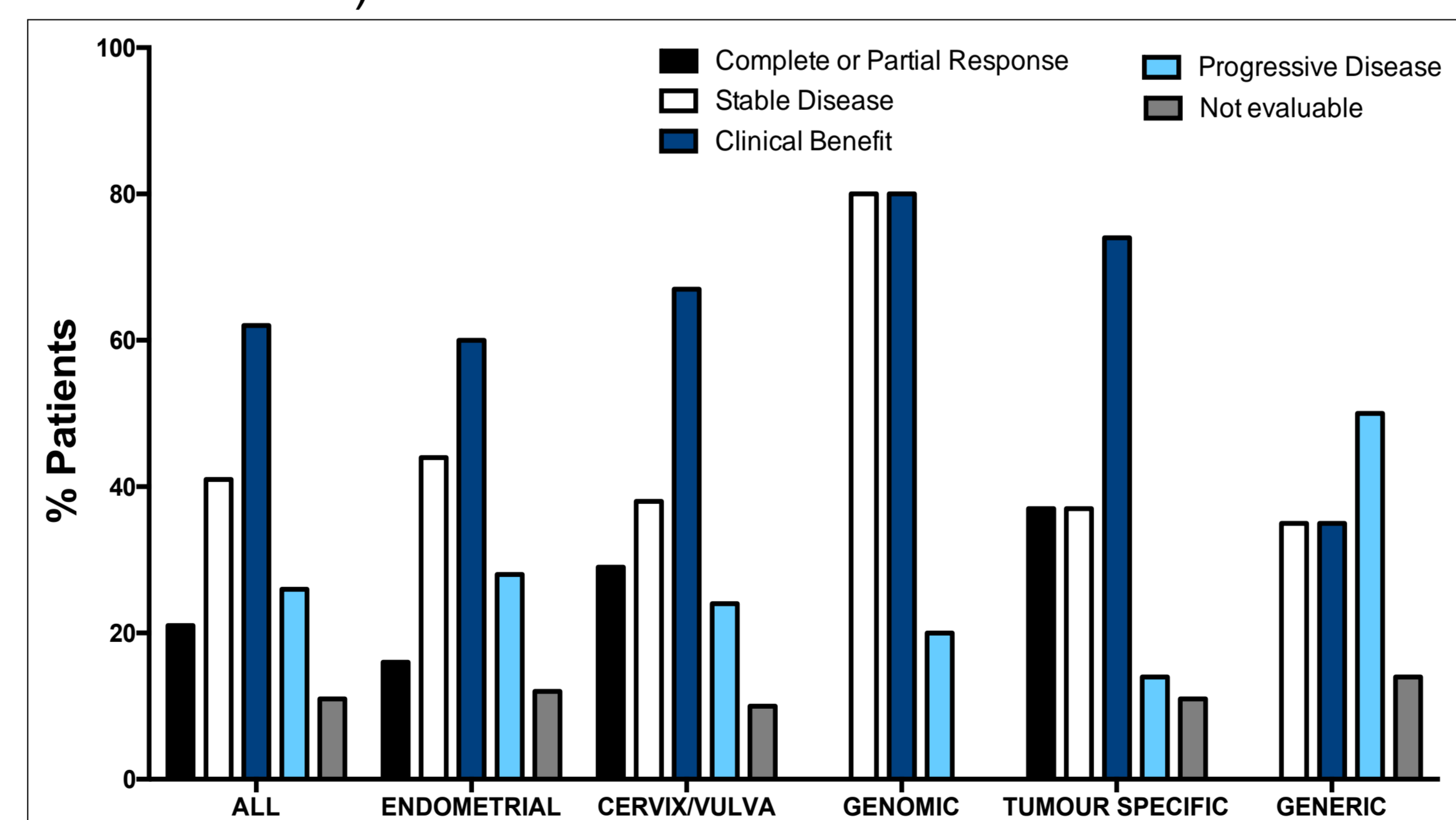


Figure 1: Response Evaluation

Outcome: Treatment Duration

- At the time of analysis, 13 (30%) patients remained on study
- Median duration on study drug:
 - 12 weeks (3-87) for all patients
 - 11 weeks (3-87) for EC and 12 weeks (5-87) for CVC patients

Outcome: Treatment Duration

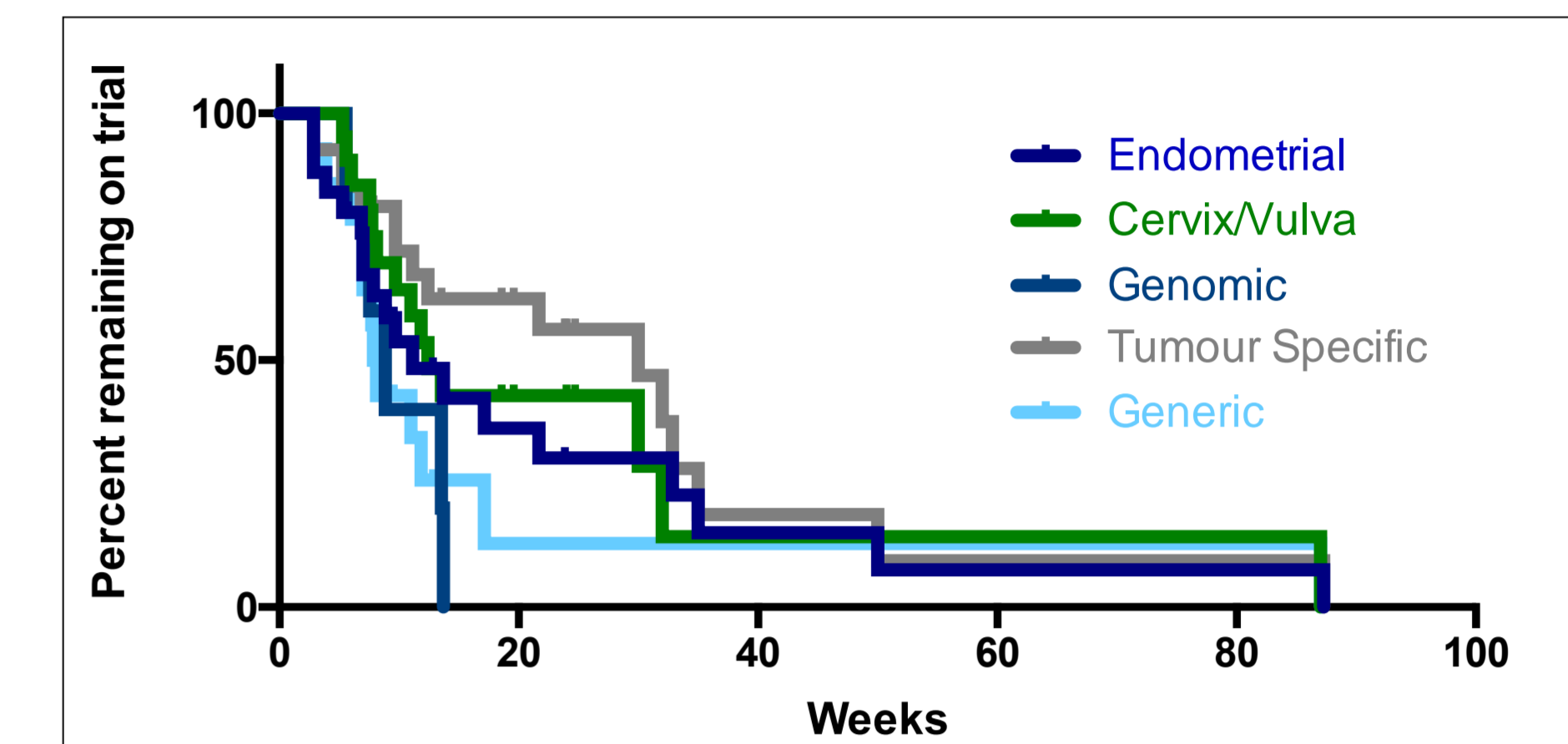


Figure 2: Treatment duration

- Duration of study treatment was significantly longer for patients treated within tumour specific cohorts (30 weeks) than either genomic or generic studies (9 and 8 weeks respectively, p=0.03 Mantel-Cox)

Outcome: Overall Survival

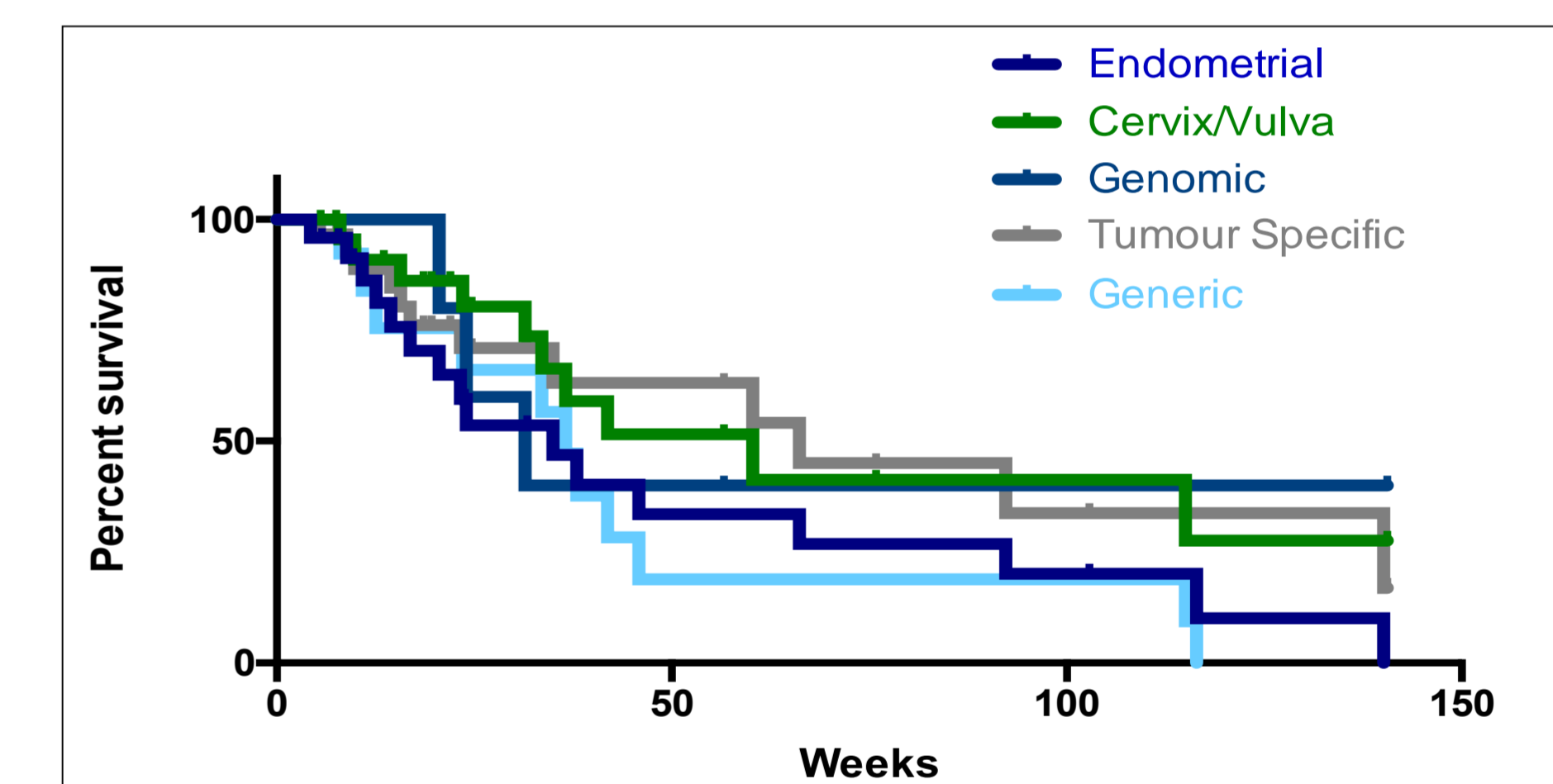


Figure 3: Overall Survival

- At the time of analysis, 24 (47%) patients remain alive
- Median overall survival:
 - 36 weeks (4-141) for all patients
 - 35 weeks (4-140) for EC and 60 weeks (6-141) for CVC patients
- Overall survival was longer for patients treated within tumour specific cohorts (66 weeks) than either genomic (31 weeks) or generic studies (37 weeks) although this did not reach significance

Conclusions

- Early phase trials represent a good option for patients with advanced EC and CVC with meaningful clinical benefit observed
- Encouraging response rates and duration of responses were observed in these patients with limited treatment options, including patients with difficult to treat subtypes such as high grade serous and carcinosarcoma EC and clear cell CVC