Multicenter phase II study of epirubicin-docetaxel (EPITAX) as first-line treatment in patients with advanced gastric cancer A GERCOR study

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Background

- Epirubicin and docetaxel combination is active in second-line treatment of patient with advanced gastric cancer resistant to cisplatin-based regimen (Louvet, ASCO 1999)

- This multicenter phase II study was performed to evaluate the efficacy and tolerance of this combination in chemo-naïve patients with advanced or metastatic gastric cancer

Objectives

- Primary endpoint
  - Response Rate
- Secondary endpoints
  - Tolerance
  - PFS
  - Overall Survival

Eligibility Criteria

- Histologically proven gastric adenocarcinoma
- Locally advanced or metastatic disease
- No prior chemotherapy.
- Measurable or evaluable disease
  (RECIST criteria)
- 18 to 75 yrs old, WHO performance status ? 2
- Adequate function of bone marrow, heart, kidney and liver
- Signed informed consent
- At least 3 month life expectancy

Methods

Epirubicin 60 mg/m^2 IV infusion over 30 mn, d1, followed 1 h later by
docetaxel 75 mg/m^2 IV over 60 mn, d1, q3w

- GCSF was administered from d3 to d9
- Corticosteroids (Prednisolone 50 mg/d) from d-1 to d4
- Efficacy was evaluated after first 3 cycles, then every 3 cycles
- Tolerance evaluation after each cycle
- 6 cycles were initially planned, then treatment could be continued in function of the tolerance and response
- 2nd line treatment with CDDP-5FU was recommended at progression

Patient characteristics

- N = 36
- Median age : 54 yrs (range: 29 - 75 yrs)
- Male / female: 29 / 7 (Sex ratio 4:1)
- PS 0: 12 pts (33.3%)
  1: 18 pts (50.0%)
  2: 6 pts (16.7%)
- Locally Advanced / Metastatic: 7 / 29 (20% / 80%)
- Tumor related symptoms (%): pain (39), anorexia (39), dysphagia (22), ascite (11)
- Metastatic sites (n): liver (19), lung (5), bone (3), lymph node (4), peritoneum (5), other (18)

Toxicity grade 3-4 per patient (NCI-CTC)

- Adverse events

Adverse events	G 3	G 4	G3+G4 (%)
Neutropenia	1	13	14 (38.9)
Thrombocytopenia	2	0	2 (5.6)
Anemia	3	1	4 (11.1)
Nausea/vomiting	5	0	5 (13.9)
Diarrhea	2	0	2 (5.6)
Stomatitis	0	0	0 (0.0)

- No treatment-related death

Response Rate

- All patients were evaluable for toxicity and response
- Median: 4 cycles (range 1 to 9) Total: 174 cycles

• Complete response (CR):	1	(2.7%)	
• Partial response (PR):	6	(16.7%)	
• Overall response (OR):	7	(19.4 %)	(95% CI: 0.07-0.32)
• Stable disease (SD):	10	(27.8%)	
• Progressive disease (PD):	19	(52.8%)	

- Symptoms improvement: 30% at first evaluation (after 3 cycles)

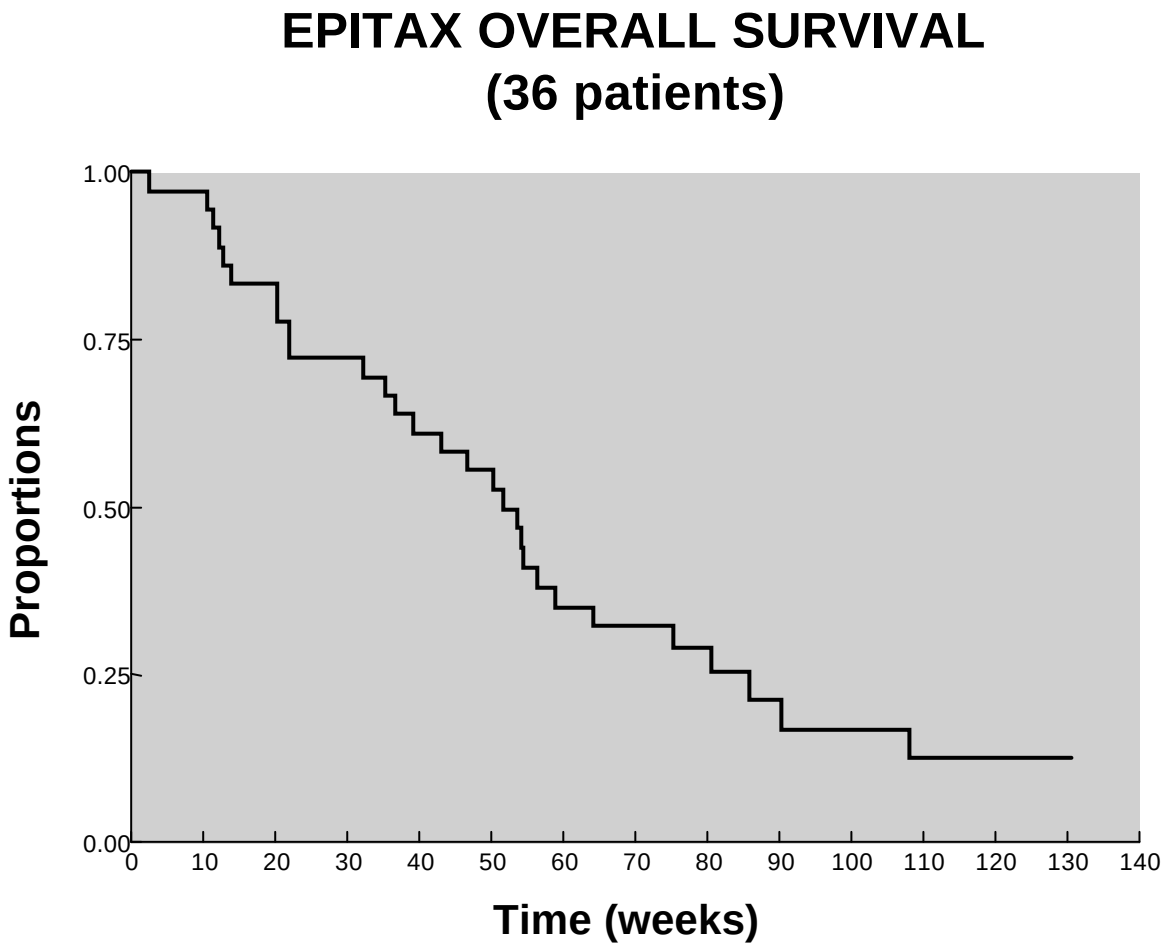
PFS, Overall Survival

- Median follow-up time: 51 weeks

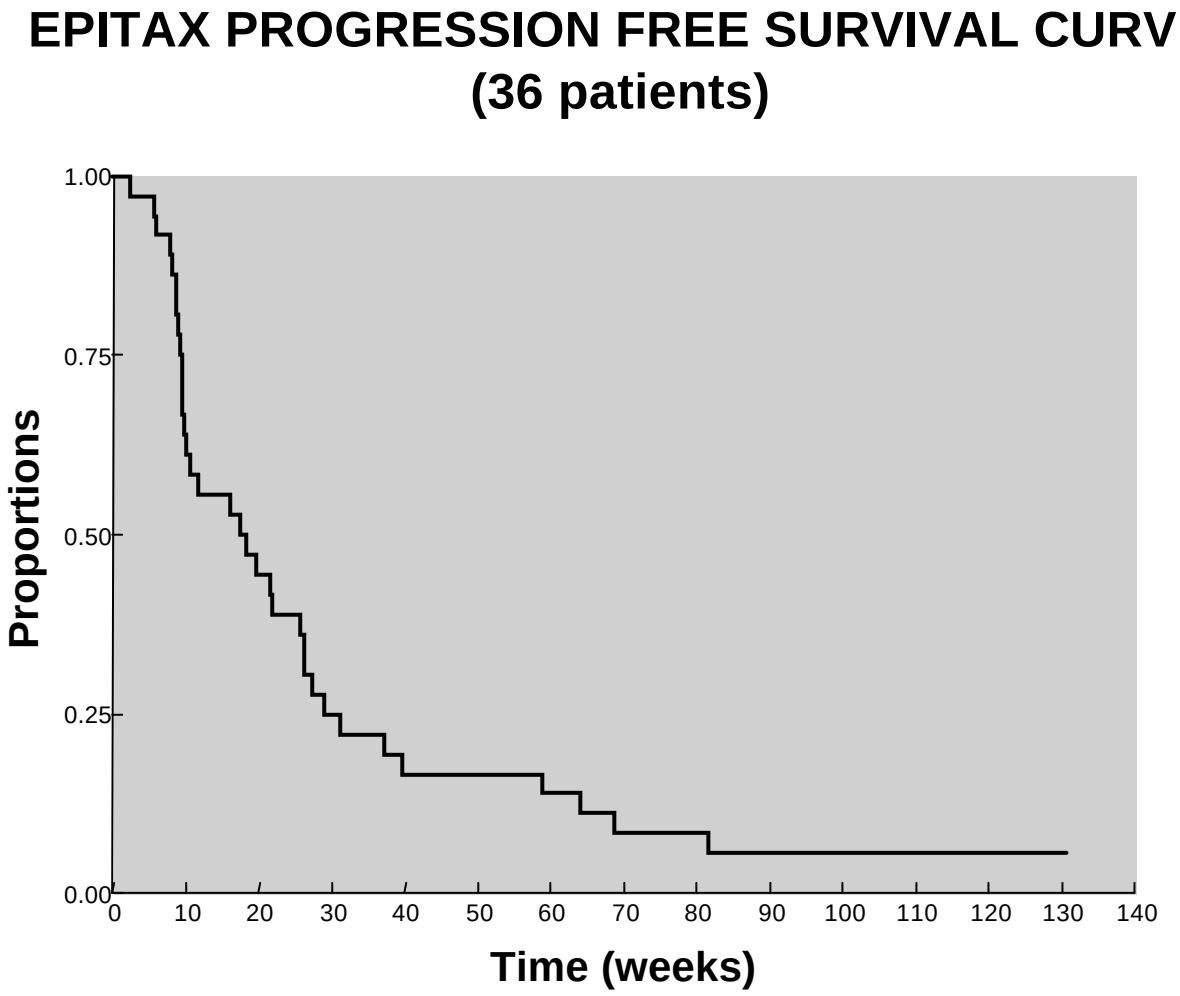
- Progression free survival (PFS): median 18 weeks (4.5 m)
  (95% CI: 0.09-0.26)
- Overall survival (OS): median 52 weeks (12 m)
  (95% CI: 0.36-0.60)

- Second-line treatment: 22/36 pts (61%) received second-line chemotherapy, the majority (19 pts) with platinum-5 FU based regimen
- Third-line treatment: 11 pts

Overall Survival



Progression-Free Survival



Conclusions

- 1/ With a 19% RR, Epitax has a moderate activity in first-line treatment of advanced gastric cancer (AGC).
- 2/ This RR is in the same range that was observed in 2nd line treatment, suggesting a non-cross resistance of Epitax with 5FU-cisplatin based combination.
- 3/ The prophylactic use of GCSF allows acceptable hematological tolerance. Other toxicity are mild.
- 4/ Two-third of patients were able to receive second-line treatment.
- 5/ The satisfactory 12 month median survival could be in part explained by early evaluation and active non-cross resistant 2nd line treatment. This point could be taken into account in the design of future studies in AGC.