A RANDOMIZED PLACEBO-CONTROLLED PHASE II STUDY WITH THE CANCER VACCINE IGN101 IN PATIENTS WITH EPITHELIAL CANCERS

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Study Sponsor:
Igeneon Krebs-Immuntherapie Forschungs- und Entwicklungs AG, Vienna, Austria

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IGN101 Background

- IGN101 is a vaccine designed for therapeutic vaccination against cancers of epithelial origin by triggering an immune response that may attack epithelial cancer cells

- A single vaccination dose consists of 500 µg murine anti-EpCAM mAb 17-1A used as vaccine antigen and adsorbed on aluminum hydroxide for subcutaneous injection

- In Phase I and II clinical trials IGN101 has shown:
  - Excellent safety and tolerability profile
  - High immunogenicity also in late stage patients and when administered with concomitant chemotherapies
  - Reduction of the number of circulating tumor cells (EpCAM positive cells) in peripheral blood

Study Design

- Double-blind, placebo controlled Phase II trial in 240 patients with CRC, NSCLC, liver/bile duct, esophageal/gastric cancer
  - Primary endpoint:
    Hints of efficacy based on overall survival of the whole study population and of major subgroups (CRC as defined by addendum)
  - Secondary endpoints:
    Safety, tolerability and immunogenicity

Study setting

- Study Center:
  - Prof. A. Settaf, Hôpital Avicenne, Rabat, Morocco

- Laboratories:
  - Dr. Kabbaj, Gendarmerie Royale, Rabat, Morocco
  - Labconsult, University Medical Centre Freiburg, Germany

- Monitoring/Data Management:
  - Hesperion Ltd., Basel

- Statistics:
  - Prof. Kundi, University Vienna
  - Prof. Bauer, University Vienna
  - Hesperion Ltd., Basel

Key patient selection criteria

- Age ≥ 18 years

- Carcinoma Stage III or IV:
  - Colorectal cancer (CRC),
  - Non-small cell lung cancer (NSCLC),
  - Cancer of the liver, bile duct, upper GI Tract (esophageal, gastric)

- Life Expectancy ≥ 3 months

- KPS ≥ 60%

Treatment

- IGN101 or Placebo, s.c. injections:
  - Days 1, 15, 29, 57 and
  - Weeks 16, 24, 32, 40 and
  - Month 16
- Concomitant standard therapies permitted

- IGN101:
  mAb 17-1A as vaccine antigen adsorbed on aluminum hydroxide

- Placebo:
  Aluminum hydroxide suspension without vaccine antigen

Patient characteristics

- 239 pts. randomized between Sept. 2001 and July 2003

  - ITT: 239 pts
  - Evaluable: 209 pts

  - CRC: 163 pts
  - NSCLC: 38 pts
  - Gastric cancer: 31 pts
  - Bile duct: 4 pts, liver: 2 pts, esophagus: 1 pt

Demographics (ITT)

	Placebo (n=119)	IGN101 (n=120)
Age [yr]		
Mean	51.7	50.7
Minimum	21.3	18.0
Maximum	81.5	75.4
Weight [kg]		
mean	60.2	58.6
Height [cm]		
mean	165.1	164.8
Sex [%]		
male	58.0	58.3
female	42.0	41.7
KPS		
90	11 (9,2%)	10 (8,3%)
80	56 (47,1%)	52 (43,3%)
70	52 (43,7%)	57 (47,5%)
60	0	1 (0,8%)

Patient status at study end (July 2004)

- 94 pts (39.3%) still alive
- 141 pts (59.0%) died
- 4 pts. (1.7%) lost to follow-up

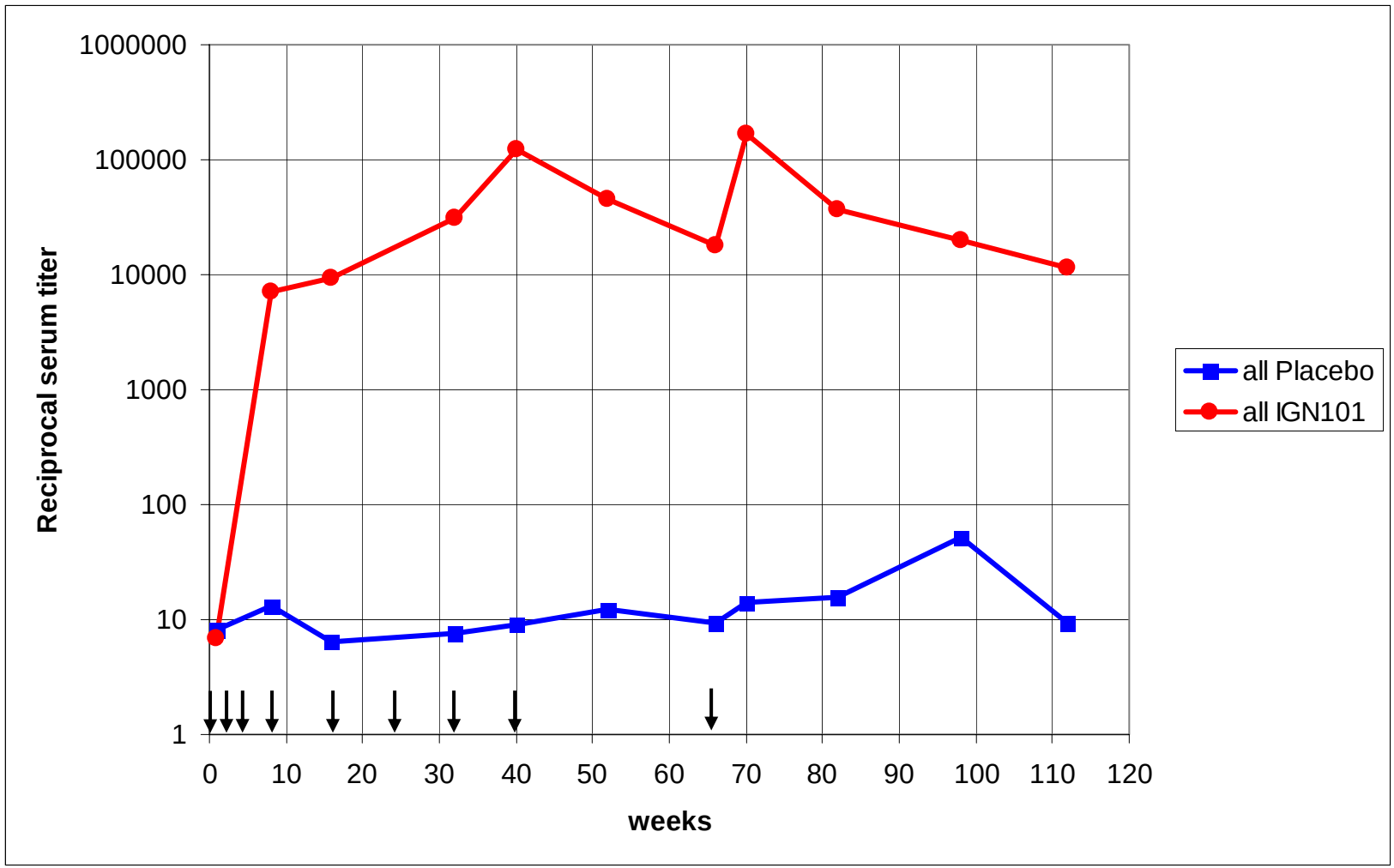
- Approx. 10% of pts received less than 4 injections (9.2% in Placebo and 12.5 % in IGN101)

Safety and tolerability

- Due to the underlying disease and concomitant therapies, a variety of typical adverse events (e.g. GI tract -, general condition, blood -, respiratory disorders) were observed

- The most frequently reported adverse events relating to study drug reported were local skin reactions (inflammation, pain, pruritus)

Immune response to IGN101



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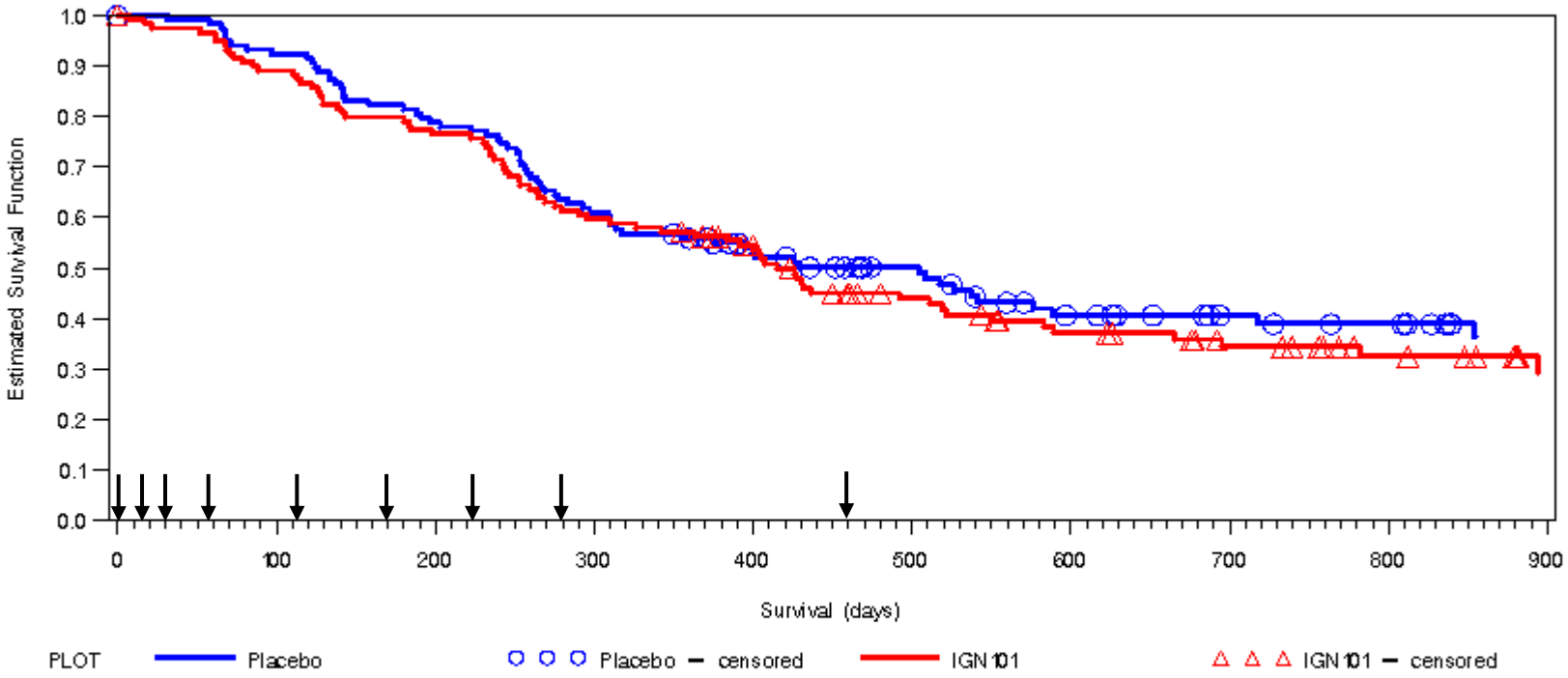
Overall survival: All indications, ITT



	Placebo	IGN101	
Number of pts	119	120	P = 0.471

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Assessment of independent prognostic factors for OS by Cox's regression analysis: All indications (ITT)

Prognostic Factor	P	Hazard Ratio
Treatment (0=Placebo,1=IGN101)	0.7028	1.076
Age (yr)	0.0126	0.979
Sex (0=Male,1=Female)	0.7385	1.071
Disease stage (0=Stage IV,1=Stage II/III)	<.0001	0.278
KPS (%) at baseline (0=≥80,1=<80)	<.0001	2.624
De-Ritis quotient (U/L) at baseline	0.0017	0.415
Albumin (G/L) at baseline	0.2136	0.974
LDH (U/L) at baseline	<.0001	1.001
Total bilirubin (U/L) at baseline	0.1338	0.971
Concomitant chemotherapy (0=no CT,1=CT)	0.9832	0.996

Patient population CRC

		Placebo	IGN101	Sum
CRC all	ITT	82	81	163
CRC all	evaluable	74	69	143
CRC IV	ITT	46	49	95
CRC IV	evaluable	40	39	79
CRC III	ITT	35	30	65
CRC III	evaluable	34	30	64
CRC II	ITT	1	2	3
CRC II	evaluable	0	0	0
C IV	ITT	25	17	42
C IV	evaluable	22	11	33
R IV	ITT	21	32	53
R IV	evaluable	18	28	46

ITT = all randomized pts
Evaluable = at least the first 4 vaccinations, Stage III or and Stage IV

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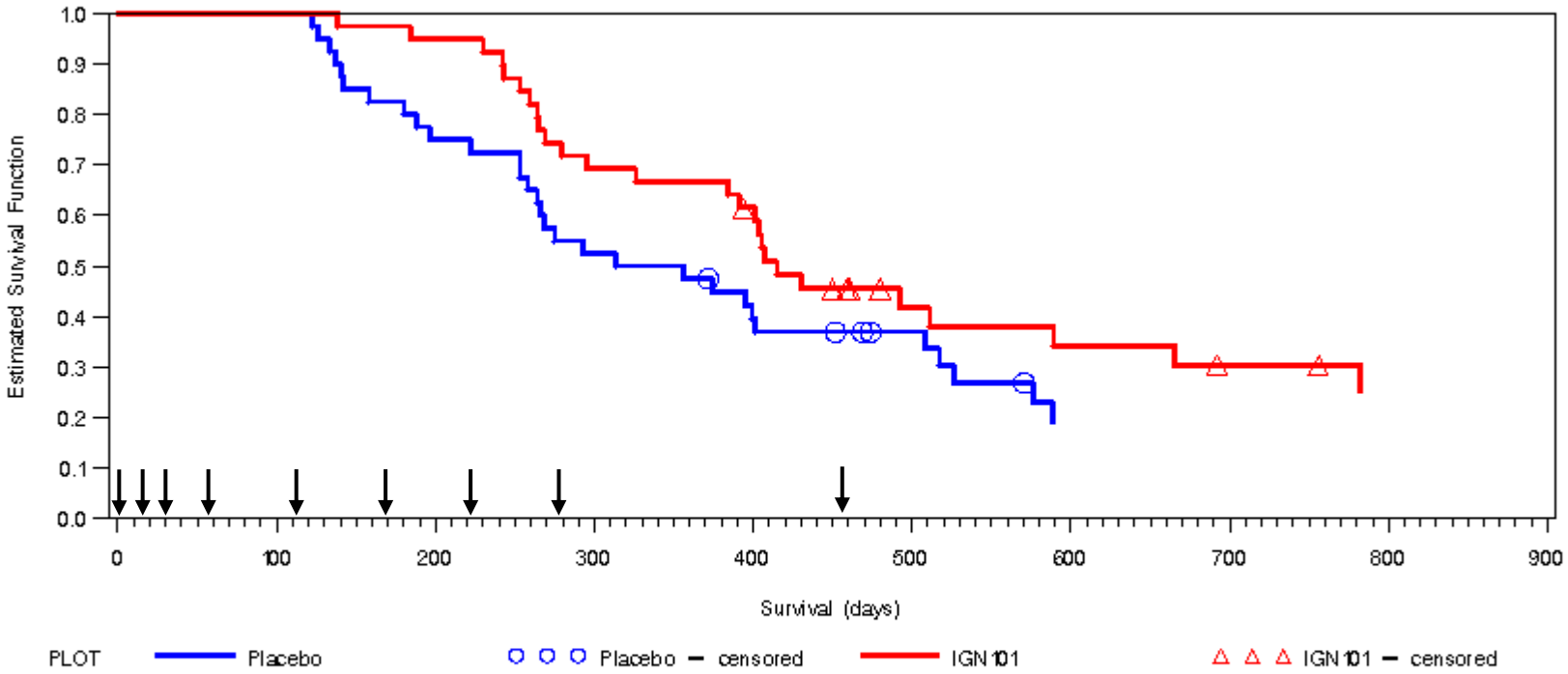
- CRC III has not enough events for analysis

=> Focus on CRC IV for further analysis

CRC stage IV (evaluable): Overall Survival



	Placebo	IGN101	
Number of pts.	40	39	
Median survival (days)	335	415	P = 0.154 (log-rank)
1 year survival (%)	47.5	66.7	P = 0.059 (log-rank)
6 month survival (%)	80.0	97.4	P = 0.015 (log-rank)

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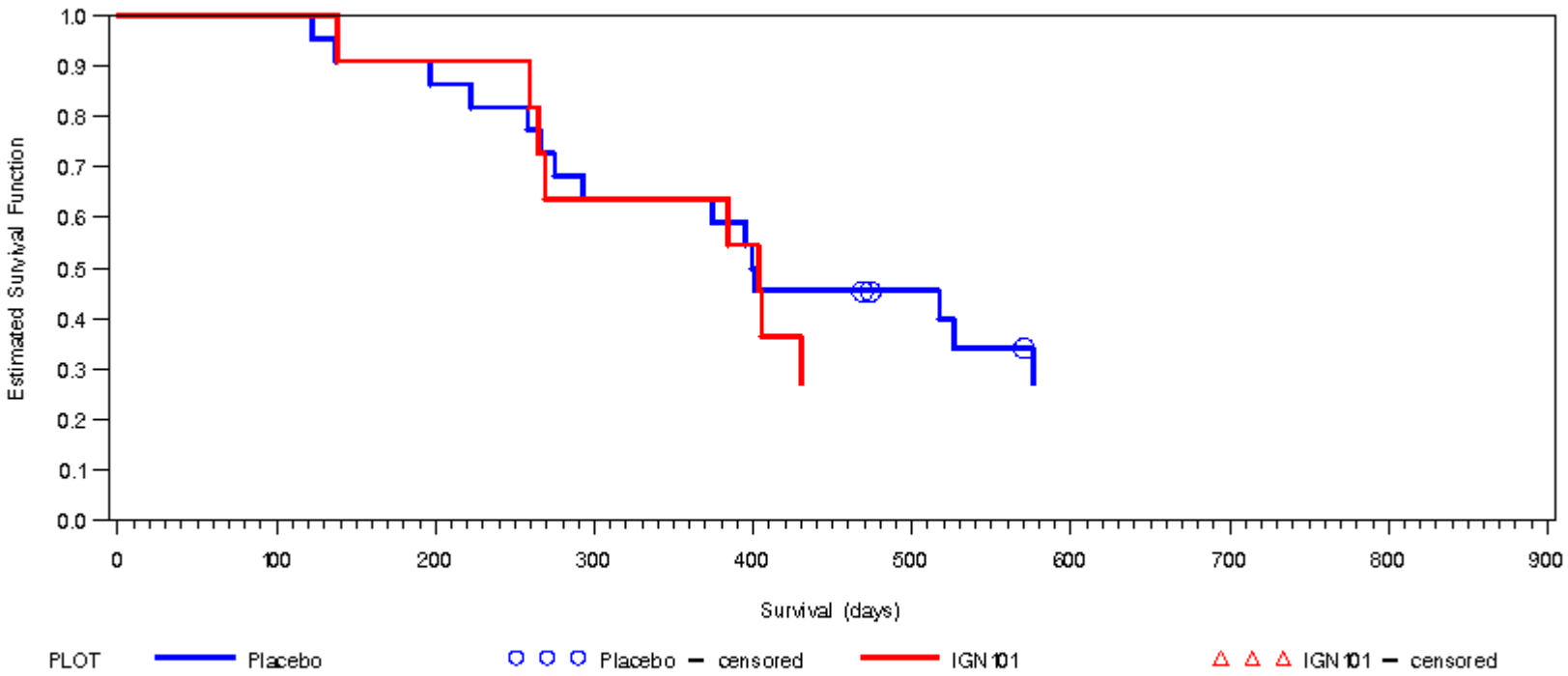
Colon cancer stage IV (evaluable): Overall survival



	Placebo	IGN101	
Number of pts.	22	11	
Median survival (days)	400	403	P = 0.805 (log-rank)

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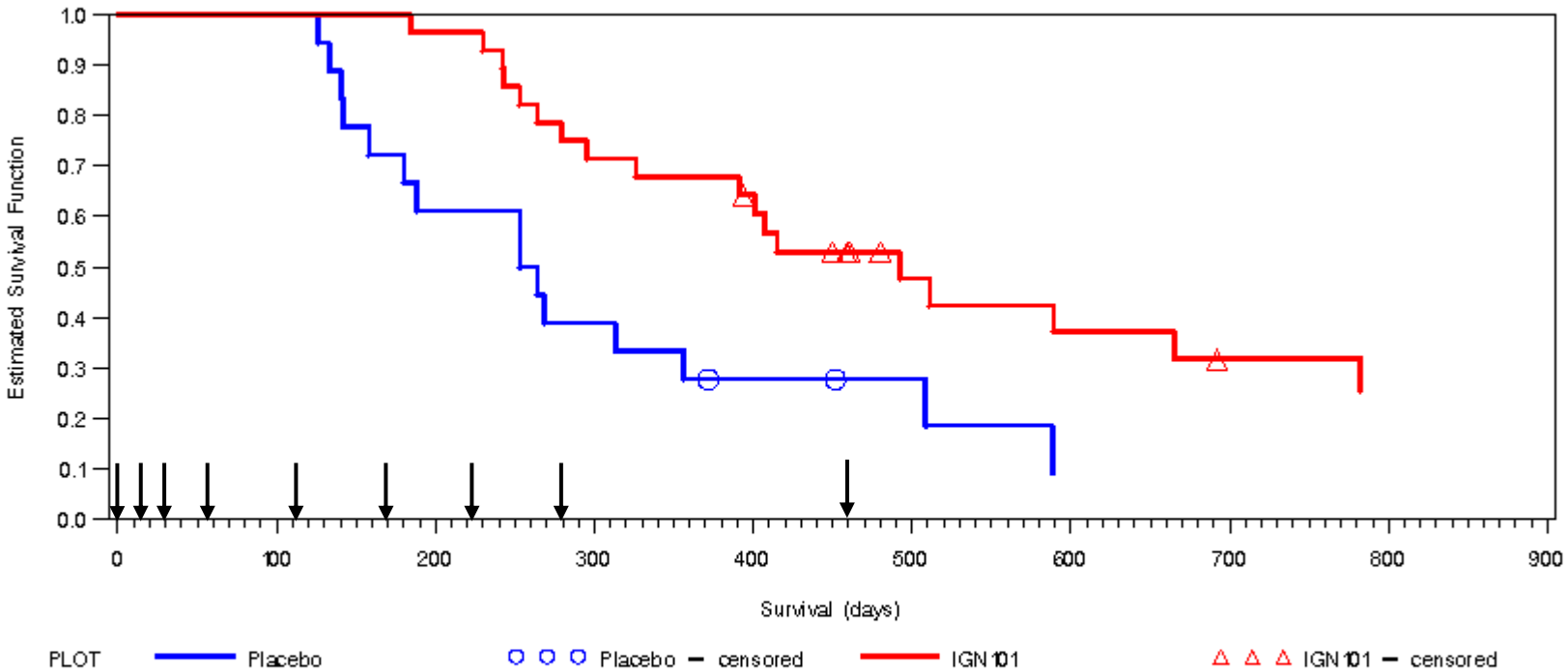
Rectal cancer stage IV (evaluable): Overall survival



	Placebo	IGN101	
Number of pts.	18	28	
Median survival (days)	259	492	P = 0.011 (log-rank)
1 year survival (%)	27.8	67.9	P = 0.003 (log-rank)
6 month survival (%)	66.7	100	P = 0.001 (log-rank)

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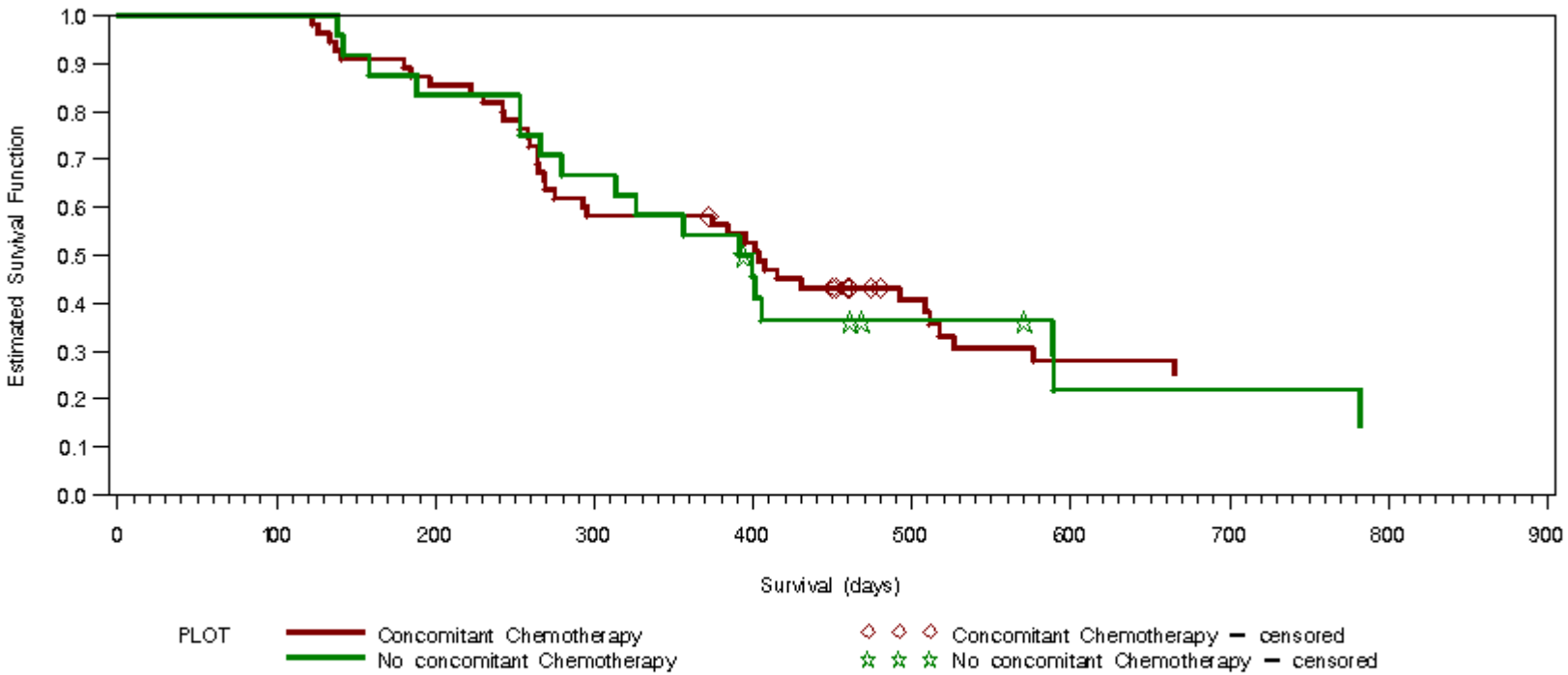
Influence of concomitant chemotherapy on survival of evaluable colorectal cancer pts. stage IV



	CT	no CT	
Number of pts.	55	24	P=0,699

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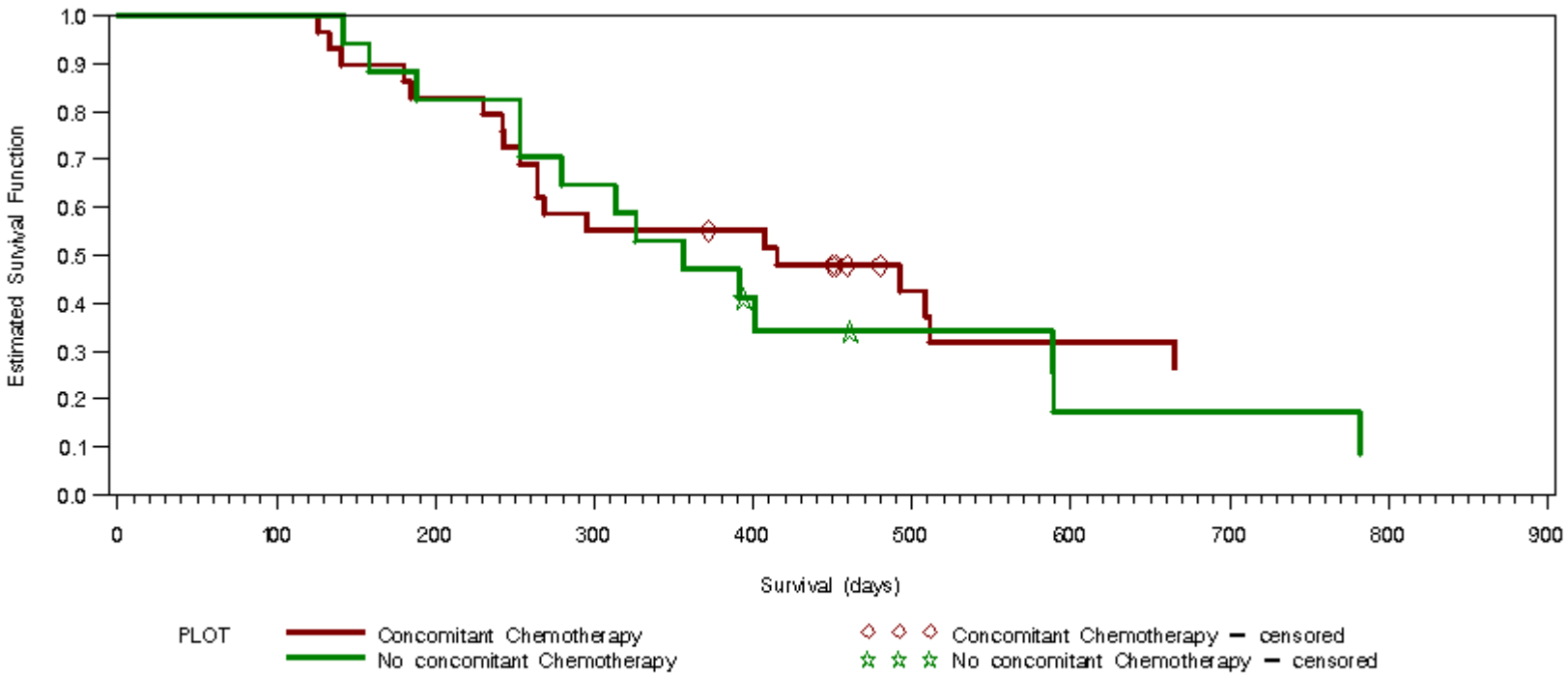
Influence of concomitant chemotherapy on survival of evaluable rectal cancer pts stage IV



	CT	no CT	
Number of pts.	29	17	P=0,454

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Influence of concomitant radiotherapy on survival of evaluable rectal cancer pts stage IV

- Placebo: 1/21 = 4.8%
- IGN101: 2/32 = 6.3%

⇒ Due to the limited number of cases with radiotherapy, influence of radiotherapy on overall survival can be neglected

Balance of further prognostic parameters on evaluable rectal cancer stage IV patients

De-Ritis quotient (ALAT/ASAT)

Placebo: 0.66 (U/l)

IGN101: 0.84 (U/l)

Karnofsky (mean values in %)

Placebo: 72.78

IGN101: 76.07

Summary and Conclusions

- IGN101 is well tolerated and safe in the tested patient population
- No survival advantage is found in all randomized pts
- A trend for a survival benefit is observed in colorectal cancer pts stage IV
- A statistically significant survival prolongation is seen in the subgroup of rectal carcinoma pts. stage IV
- Based on these results, a sufficiently powered confirmatory trial is warranted

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