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MEETING SUMMARY

ASCO 2016: JUNE 3RD TO 7TH 2016
WCGIC 2016: JUNE 28TH TO JULY 2ND 2016

BY DR. ANDREA SARTORE BIANCHI – MILANO, ITALY

CANCERS OF THE UPPER GI TRACT

A MULTICENTER RANDOMIZED PHASE III TRIAL OF NEO-ADJUVANT CHEMOTHERAPY FOLLOWED BY SURGERY AND CHEMOTHERAPY OR BY SURGERY AND CHEMORADIOTHERAPY IN RESECTABLE GASTRIC CANCER

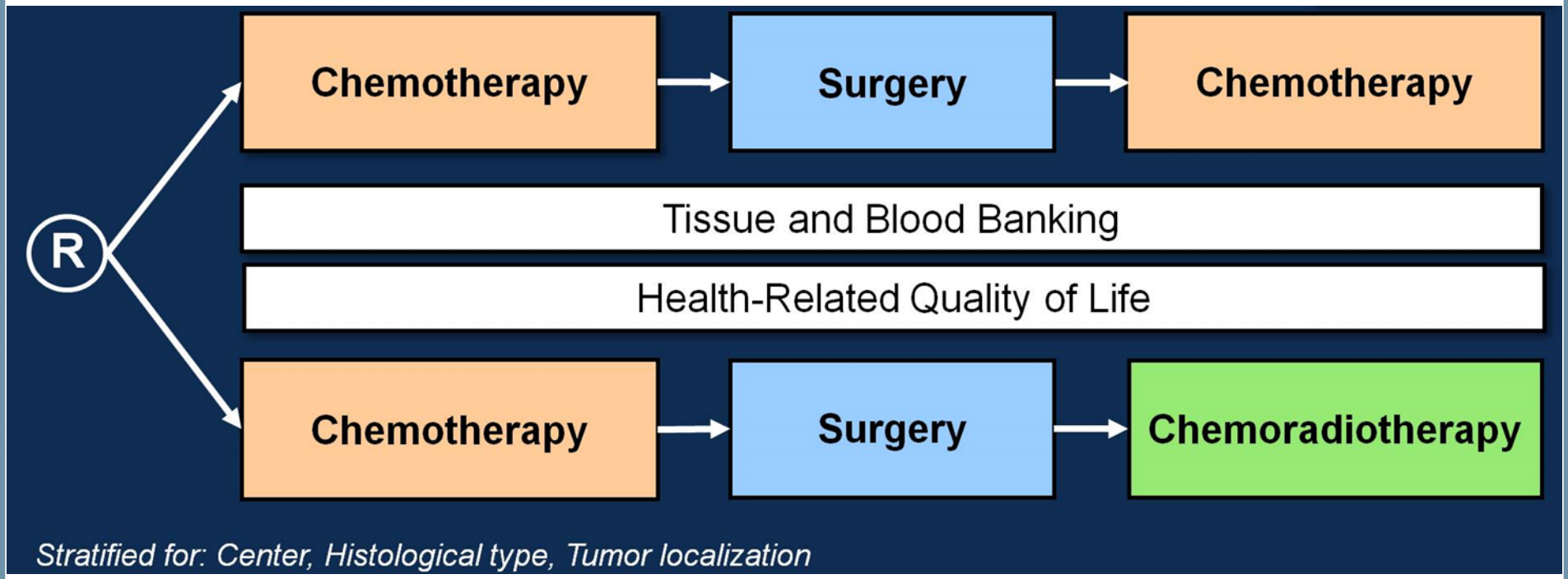
FIRST RESULTS FROM THE CRITICS STUDY

Marcel Verheij[1], EPM Jansen[1], A Cats[1], NCT van Grieken[2], H Boot[1], PA Lind[3], E Meershoek-Klein Kranenbarg[4], M Nordsmark[5], HH Hartgrink[4], H Putter[4], AK Trip[1], JW van Sandick[1], K Sikorska[1], H van Tinteren[1], YHM Claassen[4], CJH van de Velde[4], on behalf of the CRITICS Investigators

[1]Netherlands Cancer Institute, [2]VU University Medical Center, [3]Karolinska University Hospital, [4]Leiden University Medical Center, [5]Århus University Hospital

Presented by Marcel Verheij at the 2016 ASCO Annual Meeting

TRIAL DESIGN



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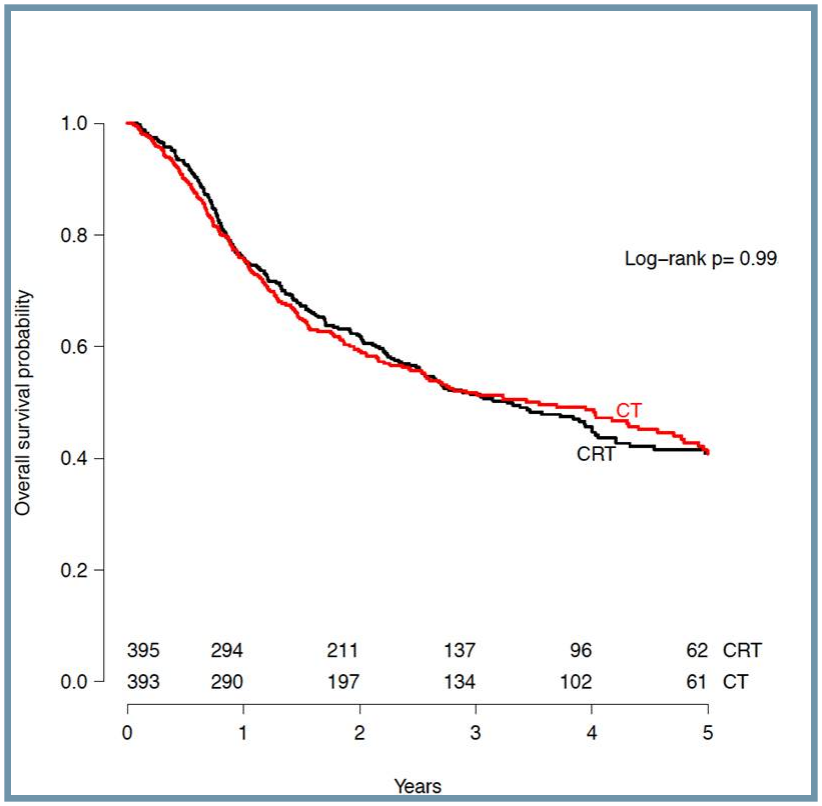
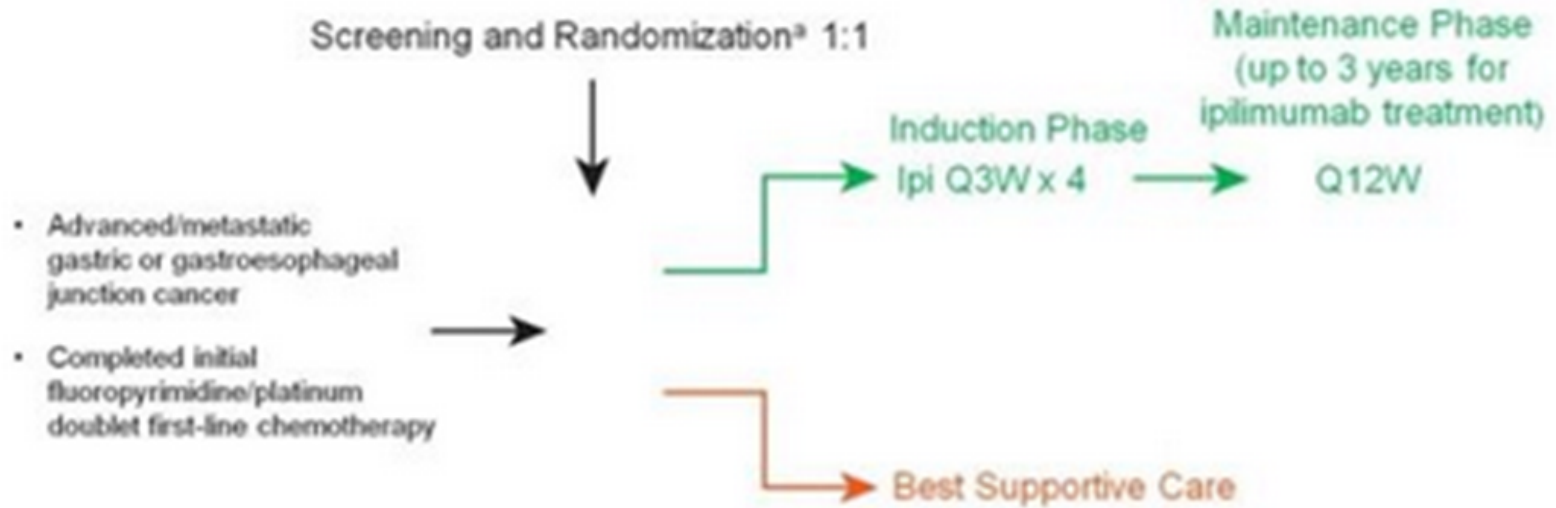
RESULTS: OVERALL SURVIVAL



	CT	CRT
5-year OS (%)	40.8	40.9
Median OS (yrs)	3.5	3.3

Presented by Marcel Verheij at the 2016 ASCO Annual Meeting

A RANDOMIZED, OPEN-LABEL, TWO-ARM PHASE 2 TRIAL COMPARING THE EFFICACY OF SEQUENTIAL IPILIMUMAB VERSUS BEST SUPPORTIVE CARE FOLLOWING FIRST-LINE CHEMOTHERAPY IN PATIENTS WITH UNRESECTABLE, LOCALLY ADVANCED/METASTATIC GASTRIC OR GASTROESOPHAGEAL JUNCTION CANCER



- Phase 2, randomized, open-label study evaluating the safety and efficacy of ipilimumab in the treatment of advanced or metastatic gastric or gastroesophageal junction adenocarcinoma following first-line chemotherapy
- Patients with stable disease or better were assigned 1:1 to receive either intravenous ipilimumab or best-supportive care (BSC) as maintenance
- BSC could comprise continuation of fluoropyrimidine received during first-line chemotherapy (active BSC) or no active maintenance treatment

[a]Patients were stratified by geographic region and prior best response to first-line chemotherapy; Ipi = ipilimumab; Q3W = every 3 weeks; Q12W = every 12 weeks

Presented by M Moehler at the 2016 ASCO Annual Meeting

AVELUMAB (MSB0010718C;ANTI-PD-1L1) IN PATIENTS WITH ADVANCED GASTRIC OR GASTROESOPHAGEAL JUNCTION CANCER FROM JAVELIN SOLID TUMOR PHASE 1B TRIAL: ANALYSIS OF SAFETY AND CLINICAL ACTIVITY

Figure 2. JAVELIN Solid Tumor GC/GEJC cohort study design

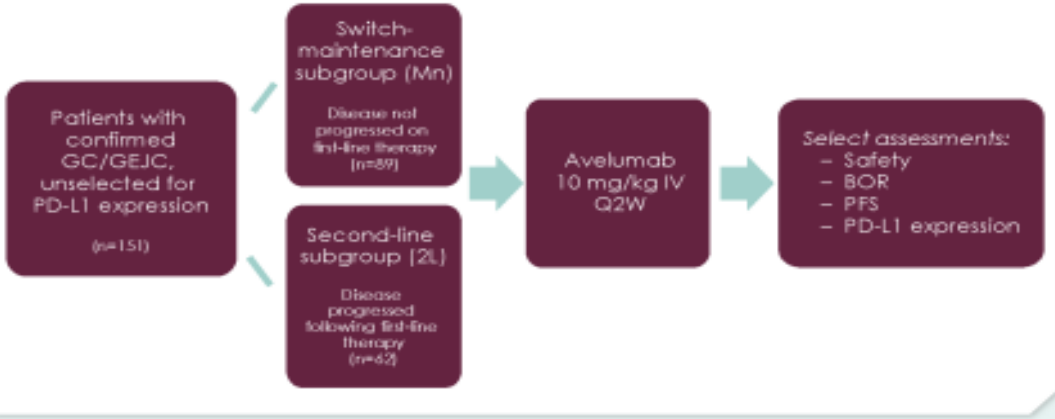


Table 5. Summary of clinical activity

Clinical activity endpoint*	Mn subgroup (N=89)	2L subgroup (N=62)
Complete response, n (%)	2 (2.2)	0
Partial response, n (%)	6 (6.7)	6 (9.7)
Stable disease, n (%)	43 (48.3)	12 (19.4)
Progressive disease, n (%)	30 (33.7)	37 (59.7)
Non-evaluable, n (%)†	8 (9.0)	7 (11.3)
ORR, % (95% CI)	9.0 (4.0, 16.9)	9.7 (3.6, 19.9)
DCR, %	57.3	29.0

CI, confidence interval; DCR, disease control rate (defined as responses + stable disease); ORR, objective response rate.

* Clinical activity of BOR based on unconfirmed and confirmed responses. Lack of response confirmation was due to no further tumor assessments at the time of cut-off or no confirmation in subsequent assessments (time-point response of SD or progressive disease). Stable disease at the first post-baseline tumor assessment after 6 weeks was required to qualify for a BOR of stable disease.

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Presented by HC Chung at the 2016 ASCO Annual Meeting

CHECKMATE-032: PHASE I/II, OPEN-LABEL STUDY OF SAFETY AND ACTIVITY OF NIVOLUMAB ALONE OR WITH IPILIMUMAB IN ADVANCED AND METASTATIC GASTRIC CANCER

Design

- Patients with stage IV G/E/GEJ tumors (n=160) unselected for PDL1 expression, range of prior therapy 0 to >3 (mostly 2-3) sequentially enrolled
  - Nivo 3mg/kg (N3)
  - Nivo 1mg/kg + Ipi 3mg/kg* (x 4 cycles), then Nivo 3mg/kg (N1+I3)
  - Nivo 3mg/kg + Ipi 1mg/kg* (x 4 cycles), then Nivo 3mg/kg (N3+I1)

Main findings

- ORR were N3: 13.6%, N1+I3: 24.5%, N3+I1: 9.6%
- PFS exhibits highest 'tail; on the N1+I3 arm
- Treatment-related >G3 AEs in 27%-45% of patients in combo arms (c/w 17% nivo only) but largely manageable and reversible
- Phase 3 trial is N1+ I3 in G/GEJ

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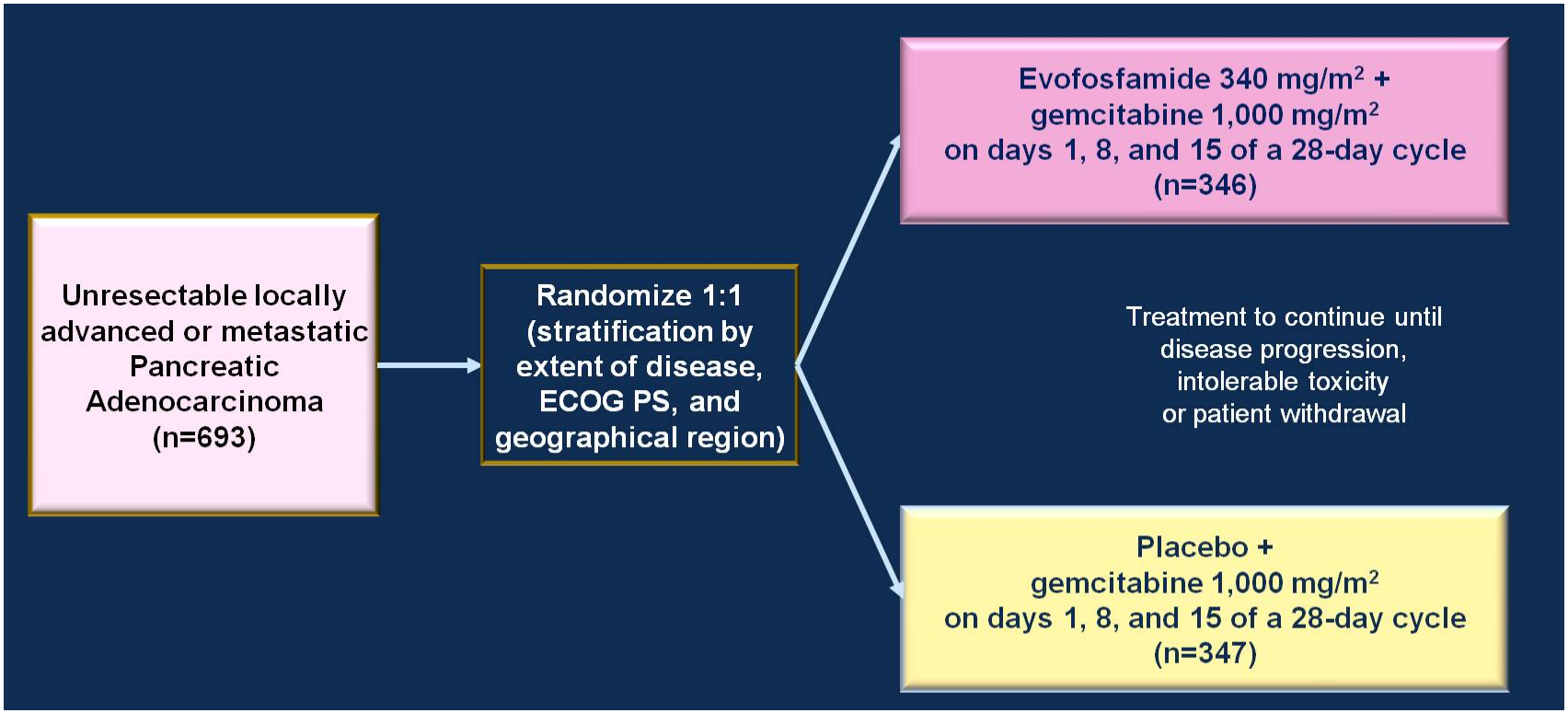
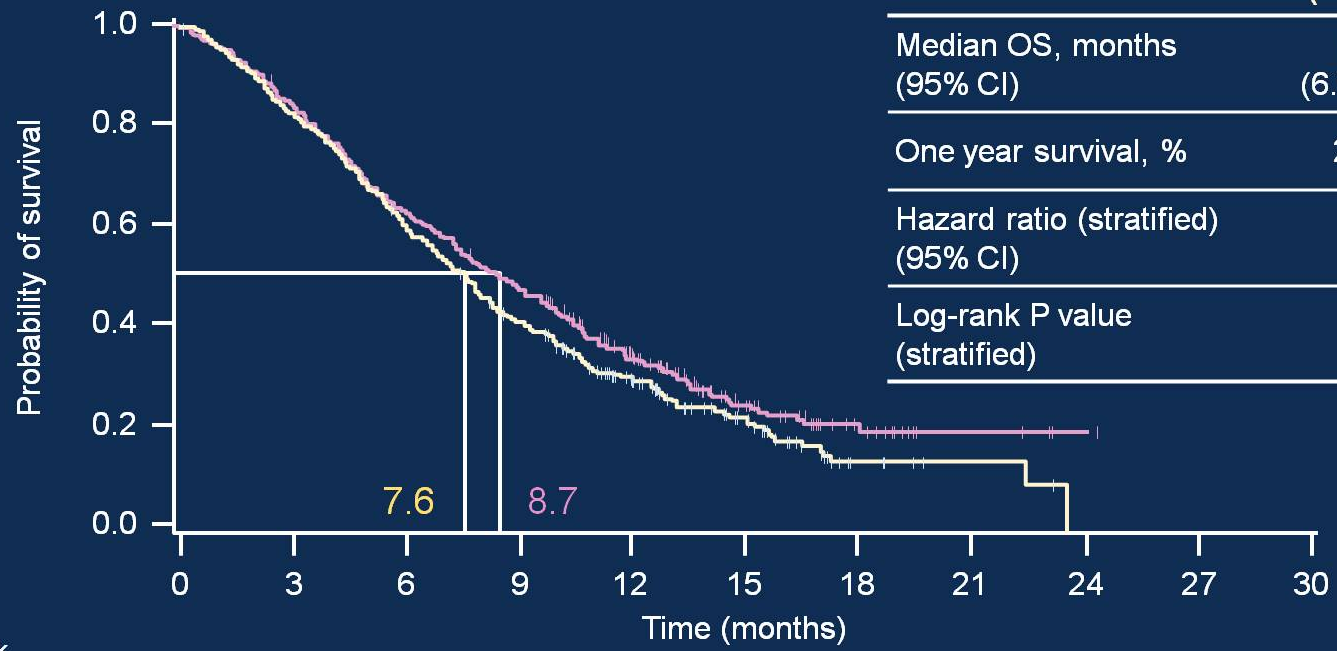
RANDOMIZED, DOUBLE-BLIND PHASE III MAESTRO DESIGN



Presented by Eric Van Cutsem at the 2016 ASCO Annual Meeting

PRIMARY ENDPOINT: OVERALL SURVIVAL ITT



	Placebo/Gem (n=347)	Evo/Gem (n=346)
Median OS, months (95% CI)	7.6 (6.7, 8.3)	8.7 (7.6, 9.9)
One year survival, %	29.8	34.2
Hazard ratio (stratified) (95% CI)	0.84 (0.71, 1.01)	
Log-rank P value (stratified)	0.059	

At risk											
Placebo/Gem	347	284	205	141	75	35	7	3	0	0	0
Evo/Gem	346	293	219	168	87	38	14	4	1	0	0

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ESPAC - 4

Stratified log-rank test with 5% 2-sided α, for a 10% difference in 2 year survival, 90% power = 480 events = 722 patients, 361 in @ arm

722 patients
pancreatic ductal adenocarcinoma
'curative' resection ≤12 wks

↓

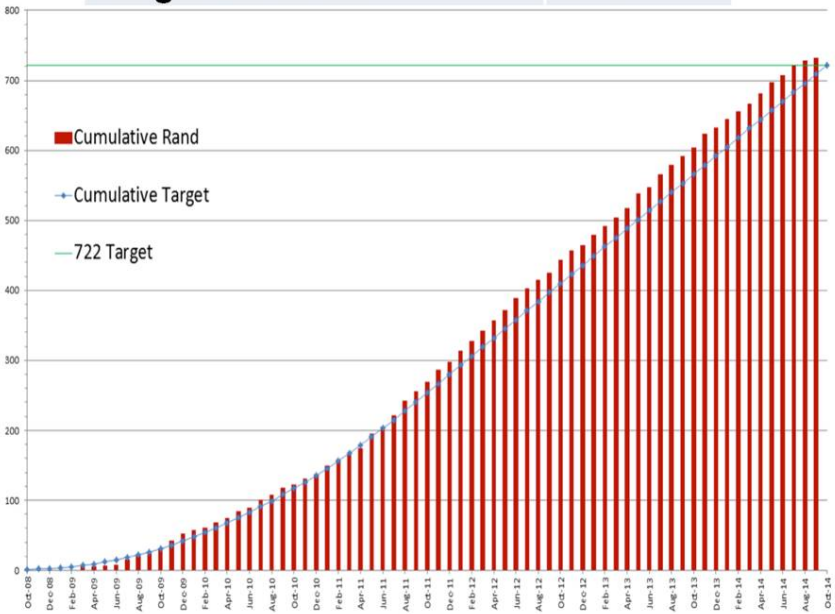
RANDOMISATION at Liverpool Cancer Trials Unit

GEMCITABINE
1000mg/m² -Days 1,8 and 15 for 6 cycles

GEMCITABINE
1000mg/m² -Days 1,8 and 15 for 6 cycles
CAPECITABINE
1660mg/m²/day – 21/28d
i.e. 24 weeks

3-MONTHLY FOLLOW UP FROM RANDOMISATION TO DEATH

Target number of patients	722
Start date	13/01/08
Number of sites opened	106
Planned close date	01/11/14
Target achieved	31/07/14



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NCRI National Cancer Research Institute
UKCRC Registered Clinical Trials Units
NHS National Institute for Health Research
CANCER RESEARCH UK

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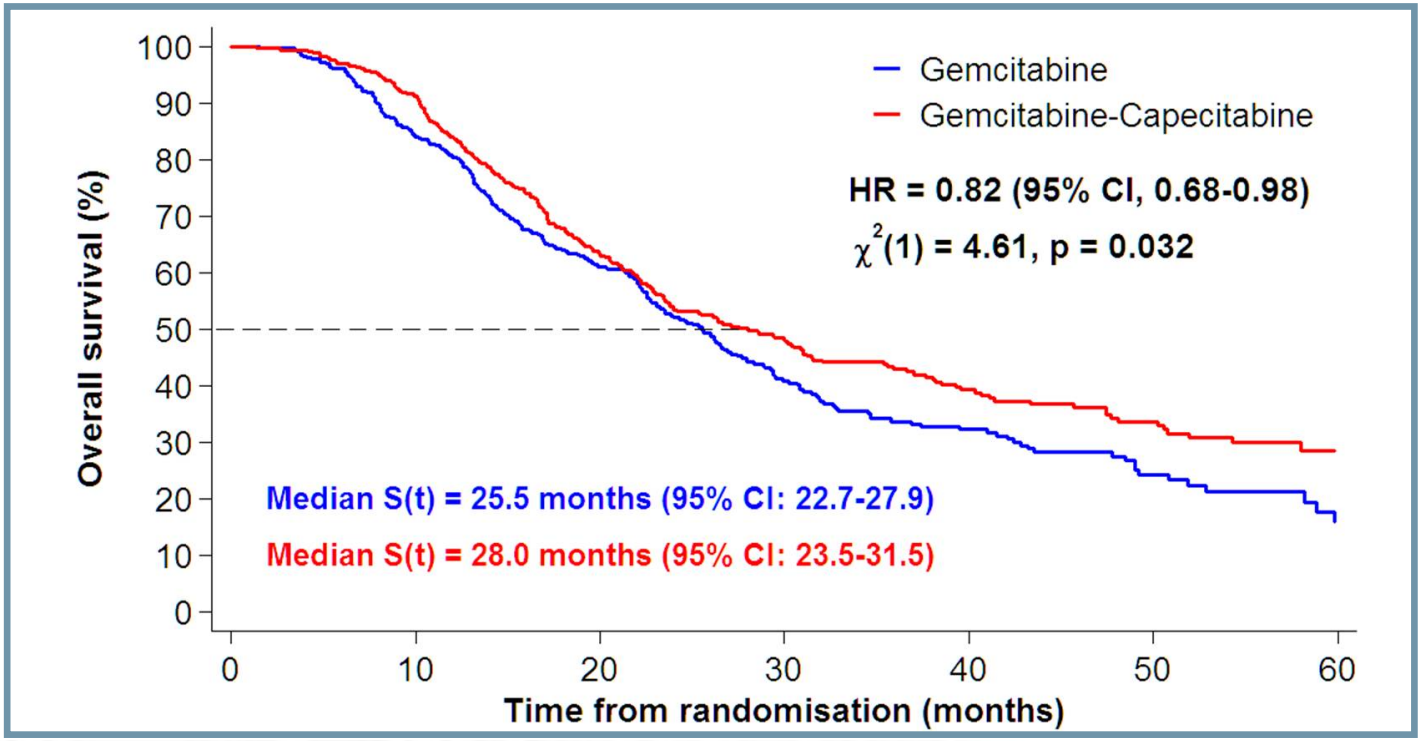
SURVIVAL BY TREATMENT



Number (%) with ≥24mth FU	80 (63%)	107 (74%)	187 (69%)

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ESPAC TRIAL: 5 YEAR OVERALL SURVIVAL

Trial	Treatment	No. of pts (N=2092)	5-Year OS (95% CI)	Stratified Log-Rank χ^2	p-value
ESPAC-1	5FU/FA	149	21 (14.6 – 28.5) %	7.03	0.030*
	No chemotherapy	143	8.0 (3.8 – 14.1) %		
	Chemoradiotherapy (5FU/Rad)	145	10.8 (6.1 – 17.0) %		
ESPAC-3	GEM	539	17.5 (14.0 – 21.2) %	0.74	0.390*
	5FU/FA	551	15.9 (12.7 – 19.4) %		
ESPAC-4	GEM	366	16.3 (10.2 – 23.7) %	4.61	0.032†
	GEMCAP	364	28.8 (22.9 – 35.2) %		

*Stratification factor: resection margin status; †stratification factors: resection margin status and country

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ABSTRACT: RESORCE TRIAL

LBA 03

Efficacy and safety of regorafenib versus placebo in patients with hepatocellular carcinoma (HCC) progressing on sorafenib: results of the international, randomized phase 3 RESORCE trial

J. Bruix[1], P. Merle[2], A. Granito[3], Y.-H. Huang[4], G. Bodoky[5], O. Yokosuka[6], O. Rosmorduc[7], V. Breder[8], R. Gerolami[9], G. Masi[10], J. Ross Paul[11], S. Qin[12], T. Song[13], J.-P. Bronowicki[14], I. Ollivier-Hourmand[15], M. Kudo[16], M.-A. LeBerre[17], A. Baumhauer[18], G. Meinhardt[19], G. Han[20] on behalf of the RESORCE Investigators 1 BCLC Group, Liver Unit, Hospital Clinic, University of Barcelona, Barcelona,
Spain 2 Groupement Hospitalier Lyon Nord, Hepatology Unit, Lyon,

RESORCE: EFFICACY AND SAFETY OF REGORAFENIB IN PATIENTS WITH HCC PROGRESSING ON SORAFENIB

Results:

- The regorafenib group had a 38% reduction in the risk of death (HR 0.62; CI 95% 0.50 – 0.78; p<0.001
- Median OS was 10.6 vs 7.8 months
- Median PFS was 3.1 vs 1.5 months
- Adverse events were consistent with the known safety profile of regorafenib

Conclusion:

- Regorafenib significantly improved OS versus best supportive care in patients with HCC who progressed after receiving sorafenib

Methods: In this double-blind, placebo-controlled trial, adults with HCC Barcelona Clinic Liver Cancer (BCLC) stage B or C who received sorafenib for ≥20 days at ≥400 mg/day and had documented radiological progression on sorafenib, Child-Pugh A liver function, and ECOG performance status 0-1 were randomized 2:1 (stratification by geographic region Asia vs rest of the world, performance status, alpha-fetoprotein, extrahepatic spread, macroscopic vascular invasion) to regorafenib 160 mg or placebo once daily during weeks 1–3 of each 4-week cycle. All received best supportive care. Treatment continued until disease progression, death, or unacceptable toxicity. The primary endpoint of overall survival (OS) was analyzed by intent-to-treat. Secondary endpoints were progression-free survival (PFS), time-to-progression (TTP), response rate (RR), and disease control rate (DCR).

Results: The trial was conducted in 21 countries and a total of 573 patients were randomized (regorafenib = 379; placebo = 194). Baseline demographic and disease characteristics were balanced between arms. For all patients, median age was 63 years, 88% were male, and 87% were BCLC stage C. Median (range) treatment duration was 3.6 months (0.03–29.4) for regorafenib and 1.9 months (0.2–27.4) for placebo. The regorafenib group had a 38% reduction in the risk of death (HR 0.62; 95% CI 0.50– 0.78; p <0.001); median OS (regorafenib vs placebo) was 10.6 vs 7.8 months. There was a 54% reduction in the risk of progression or death with regorafenib (HR 0.46; 95%CI 0.37–0.56; p <0.001); median PFS (regorafenib vs placebo) was 3.1 vs 1.5 months. Median TTP (regorafenib vs placebo) was 3.2 vs 1.5 months (HR 0.44; 95%CI 0.36– 0.55; p < 0.001). DCR (complete and partial responses + stable disease by mRECIST) for regorafenib vs placebo was 65.2% vs 36.1% (p < 0.001). Overall RRs (complete and partial responses) were 10.6% vs 4.1% (p = 0.005), respectively. Rates of grade ≥3 adverse events were 79.7% with regorafenib and 58.5% with placebo. Most common grade ≥3 adverse events occurring more frequently in the regorafenib group included (regorafenib vs placebo) hypertension (15.2% vs 4.7%), hand-foot skin reaction (12.6% vs 0.5%), fatigue (9.1% vs 4.7%), and diarrhea (3.2% vs 0%). Rates of dose modifications due to adverse events were 68.2% with regorafenib and 31.1% with placebo. Deaths occurring up to 30 days after last dose of study drug were higher in the placebo group (13.4% regorafenib, 19.7% placebo).

Conclusions: Regorafenib significantly improved OS in patients with HCC who progressed during treatment with sorafenib. Adverse events were consistent with the known safety profile of regorafenib.

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