Efficacy and Safety of Folfirinox in pancreatic metastatic cancer

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Introduction

Efficacy and safety of a combination chemotherapy (CT) regimen consisting of oxaliplatin, irinotecan, fluorouracil and leucovorin (**FOLFIRINOX**) have been investigated in metastatic pancreatic cancer in real practice.

Our study endpoints are:

- Objective response and disease stabilization rates
- Progression Free Survival (PFS) / Overall Survival (OS)
- Toxicities

Observatory of Cancer B PL

- Created in 2003 by Regional Representatives of French ministry of health
- Collects data from both private and public hospitals
- Provides a reflexion on drug management to optimize health care

Methods/Population description (1)

- **340 patients** included **between July 2010 and June 2012** amongst 22 private institutions and public hospitals of Brittany and Pays de la Loire

✓ **Group 1 :** 241 patients (71%) according to Prodige 4 criteria (Conroy et al, 2011).
- Age between 18-75 years
- Metastatic pancreatic adenocarcinoma (histo/cytologically confirmed)
- In metastatic first-line therapy
- Performance status score: 0 or 1
- Good haematological and renal function
- Subnormal bilirubin level (possible biliary drainage) with bili<1.5 ULN

✓ **Group 2 :** 26 patients (7%) did not respected at least one Prodige 4 criteria
- 8 : PS ≥2
- 7 : abnormal bilirubin level
- 7 : > 75 years old
- 1 : abnormal haematological function
- 1 : >75 years old / abnormal bili
- 1 : PS>1 / abnormal bili
- 1 : histo/cytologically not confirmed

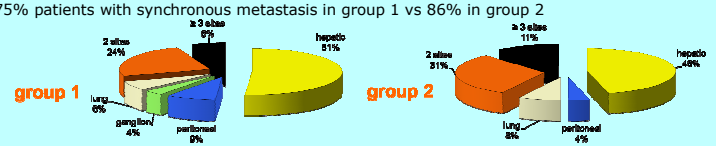
✓ **Group 3 :** 59 patients (17%) had a locally advanced cancer

✓ **Group 4 :** 14 patients (4%) have been treated in 2nd metastatic line.

- **Treatment:** oxaliplatin (85 mg/m²), leucovorin (400 mg/m²), irinotecan (180 mg/m²) and 5-FU (400 mg/m² bolus plus 2 400 mg/m² infusion over 46 hours) biweekly

Population description (2)

- 75% patients with synchronous metastasis in group 1 vs 86% in group 2



Results

	Group 1 (n=241)	Group 2 (n=26)	Group 3 (n=59)
Age ≤ 75	241 (100%)	18 (69%)	55 (93%)
PS0-1	241 (100%)	17 (65%)	55 (93%)
Good haematological/renal function	241 (100%)	25 (96%)	58 (98%)
Subnormal bilirubin level (<1.5 N)	241 (100%)	17 (65%)	51 (86%)
Men/Women	143 M / 98 WM 59% / 41%	15M / 11 WM 58% / 42%	34 M / 25 WM 58% / 42%
Median age (years)	62 [32-75]	64 [29-79]	64 [39-81]
Synchronous metastasis	181 (75%)	22 (85%)	NA
Overall Response Rate (ORR)	95 (39%)	4 (16%)	23 (39%)
Complete Response (CR)	6 (2%)	0	0
Partial Response (PR)	89 (37%)	4 (16%)	23 (39%)
Stable Disease (SD)	63 (26%)	10 (40%)	25 (42%)
Progression Disease (PD)	50 (21%)	7 (28%)	4 (7%)
Unknown	31 (13%)	5 (19%)	5 (8%)
Treatment ongoing	2 (1%)	0	2 (3%)
Median cure number	9 [1-27]	6 [1-12]	7.5 [1-20]
Dose adjustment at C1	98 (41%)	13 (50%)	29 (49%)
Dose adjustment after C1	98 (40%)	6 (24%)	20 (34%)
Grade III/IV toxicity	77 (32%)	10 (40%)	20 (34%)
PFS (months)	6.54 [5.98-7.29]*	4.14 [1.68-6.21]*	9.49 [8.74-11.47]
OS (months)	10.91 [8.94-12.02]**	7.00 [4.01-11.20]**	11.24 [9.95-15.01]

Data Base : Baseline Characteristics and clinical benefit of Patients (*p=0.0107; **p =0.0166)

Reason of folfirinox treatment arrest

	Group 1	Group 2	Group 3
End of treatment	36	1	13
Progression	82	9	6
Toxicity	22	4	7
Medical decision	63	6	24
Patient wish	10		1
Death	12	5	
Others	5		1
Treatment ongoing	*11*	*1*	*7*

For group 1, 59% of patients have received **a 2nd line** after folfirinox treatment; for group 2, 58 %; for group 3, 42 %.

Grade III and IV toxicities

	Group 1	Group 2
Digestive	29	2
Haematologic	26	4
Neurologic	20	1
Thromboembolic	6	3
Allergy	5	
Asthenia	3	1
Infection	3	
Cardiac/respiratory	3	

Differences were not significant (p=0.6189)

Progression Free Survival/Overall Survival

PFS and OS have been significantly increased when Prodige 4 criteria were respected :

OS : **10.91** months [8.94-12.02] **in gr1** vs **7.00** [4.01-11.20] **in gr2 (p =0.0166)**

PFS : **6.54** months [5.98-7.29] **in gr1** vs **4.14** [1.68-6.21] **in gr2 (p=0.0107)**

Conclusion

Our study shows a high rate of dose adjustement before the first cure (>40%) in all groups while in most cases DPD and/or UGT mutations have not been reported. What is the reason ?

Our study tends to prove that PFS and OS decrease significantly in case of non respect of Prodige 4 criteria with a lower response rate.

For group 2, with a high rate of dose adjustement, it will be interessed to compare in a prospective trial modified Folfirinox versus Gemcitabine or Gemcitabine Nab-paclitaxel.

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