ASCO 2010 Update

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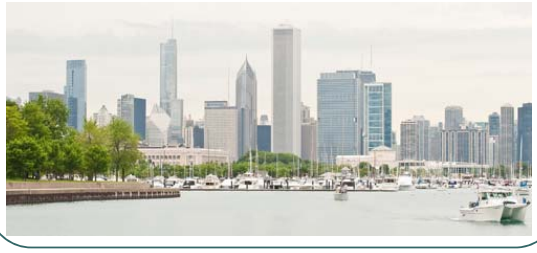
APOPC 2010

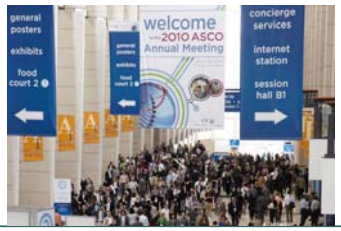
The American Society of Clinical Oncology (ASCO) 2010 Annual Meeting, which returned to Chicago this year, held June 4-8.

- "Advancing quality through innovation"



The American Society of Clinical Oncology (ASCO) 2010 Annual Meeting, which returned to Chicago this year, held June 4-8.

- More than 32,000 clinicians, researchers, and top experts from more than 100 countries attended



Advanced Non Small Cell Lung Cancer

ALK Inhibitor Crizotinib Safe and Highly Active in ALK-Positive NSCLC
"Plenary Presentation"

Bang Y, Kwak EL, Shaw AT, et al. Clinical activity of the oral ALK inhibitor, PF-02341066, in ALK-positive patients with non-small cell lung cancer (NSCLC). Program and abstracts of the 2010 Annual Meeting of the American Society of Clinical Oncology; June 4-8, 2010; Chicago, Illinois. Abstract 3.

Background

- ALK fusion protein
  - Caused by chromosomal inversion and/or translocation
  - Potentially oncogenic
    - Implicated in tumor cell survival and proliferation pathways

ALK = anaplastic lymphoma kinase

Background

- ALK-positive NSCLC
  - *EML4-ALK* fusion gene expressed in approximately 5% of NSCLC Potentially oncogenic
  - ALK inhibition associated with substantial tumor regression in preclinical NSCLC animal model [1]
  - No apparent response to epidermal growth factor receptor inhibition [2]

1. Soda M, et al. Identification of the transforming EML4-ALK fusion gene in non-small-cell lung cancer. Nature. 2007;448:561-566; 2. Shaw AT, et al. Clinical features and outcome of patients with non-small-cell lung cancer who harbor EML4-ALK. J Clin Oncol. 2009;27:4247-4253.

Background

- Crizotinib (PF-02341066)
  - Dual selective inhibitor of ALK and c-MET
  - ATP-competitive inhibitor
  - Orally available small molecule
- Potent inhibition of cell growth and induction of apoptosis in NSCLC cell lines
- Demonstrated safe in dose-escalation study[1]

1. Tan W, Wilner KD, Bang Y, et al. Pharmacokinetics (PK) of PF-02341066, a dual ALK/MET inhibitor after multiple oral doses to advanced cancer patients. Program and abstracts of the 2010 Annual Meeting of the American Society of Clinical Oncology; June 4-8, 2010; Chicago, Illinois. Abstract 2606.

ALK Inhibitor Crizotinib Safe and Highly Active in ALK-Positive NSCLC

Current study evaluated safety and efficacy of crizotinib specifically in ALK-positive NSCLC patients

Ongoing, single arm, first-in-patient study

Schematic of Study Design

- Data for first 82 patients recruited into an expanded cohort from dose-escalation study
- Patients treated at recommended phase II dose
  - 250 mg twice daily

Schematic of Study Design

- Response determined using response evaluation criteria in solid tumors with radiographic scans
  - Repeated every 8 weeks

Eligibility

- Patients with ALK-positive NSCLC
  - ALK fusion determined by fluorescence in situ hybridization
  - No limits to previous treatment
  - Treated brain metastases allowed

Baseline Characteristics

Characteristic	ALK-Positive NSCLC Patients (N = 82)
Male, %	43
Mean age, yrs (range)	51 (25-78)
Race, %	
• White	56
• Asian	33
ECOG performance score, %	
• 0	29
• 1	54
• 2	16
• 3	1
Smoking status, %	
• Never	76
• Former	23
• Current	1

Baseline Characteristics

Characteristic	ALK-Positive NSCLC Patients (N = 82)
Histology, %	
▪ Adenocarcinoma	96
▪ Squamous cell carcinoma	1
▪ Other	2
Number of previous treatments, %	
▪ 0	6
▪ 1	33
▪ 2	18
▪ ≥ 3	41

Main Findings

- Crizotinib active in ALK-positive NSCLC patients
  - Confirmed ORR in 57% of patients (95% CI: 46% to 68%)
    - 57% ORR in patients with ECOG performance score 2 or 3

Main Findings

- Duration of response: 1-15 months
- Disease control rate at 8 weeks: 87% (95% CI: 77% to 93%)

Main Findings

- ORR to crizotinib declined with increasing number of previous therapies received
  - 80% with no previous treatment
  - 52% with 1 previous regimen
  - 67% with 2 previous regimens
  - 56% with ≥ 3 previous regimens

Main Findings

- PFS
  - 6-month PFS: 72% (95% CI: 61% to 83%)
  - Median PFS not yet reached
  - 70% of patients in follow-up for PFS
  - Median follow-up: 6.4 months

Other outcomes

- Crizotinib well tolerated, with few treatment-related grade 3/4 adverse events reported

Other outcomes

- Any grade 3/4 adverse event: 13%
  - Elevated alanine aminotransferase: 6%
  - Elevated aspartate aminotransferase: 6%
  - Lymphopenia: 2%
  - Hypophosphatemia: 1%
  - Neutropenia: 1%
  - Hypoxia: 1%
  - Dyspnea: 1%
  - Pulmonary embolism: 1%

Other outcomes

- Treatment-related grade 1/2 adverse events reported in ≥ 10% of patients, primarily gastrointestinal events and visual disturbance

Other outcomes

- Nausea: 54%
- Diarrhea: 48%
- Vomiting: 44%
- Visual disturbance: 42%
  - Defined as changes in light/dark accommodation with no abnormalities upon ophthalmologic exam
- Constipation: 24%
- Peripheral edema: 16%
- Dizziness: 15%
- Decreased appetite: 13%
- Fatigue: 10%

Other outcomes

- Majority of patients (77%) remain on crizotinib
  - Median duration of treatment: 5.7 months
- Reasons for discontinuation of crizotinib
  - Treatment-related adverse event (n = 1)
  - Unrelated adverse event (n = 1)
  - Unrelated death (n = 2)
  - Other (n = 2)
  - Disease progression (n = 13)

Summary of Key Conclusions

- Crizotinib active in patients with anaplastic lymphoma kinase (ALK)–positive non-small-cell lung cancer (NSCLC)
  - ORR: 57%
  - 6-month PFS rate: 72%
  - Response or SD (ie, disease control) in majority (87%) of patients

Summary of Key Conclusions

- Few serious adverse events reported
  - Most toxicity related to mild or moderate gastrointestinal events or visual disturbances

Summary of Key Conclusions

- High response to crizotinib in this population of largely pretreated NSCLC patients suggests crizotinib may become a potential new standard of care for ALK-positive patients
  - Supports development of targeted therapies in NSCLC

Summary of Key Conclusions

- Phase III study initiated to compare crizotinib with standard-of-care chemotherapy (pemetrexed or docetaxel) in ALK-positive NSCLC

Advanced Non Small Cell Lung Cancer

TORCH: international, multicenter, randomized phase III trial[1]

1. Gridelli C, Ciardiello F, Feld R, et al. International multicenter randomized phase III study of first-line erlotinib (E) followed by second-line cisplatin plus gemcitabine (CG) versus first-line CG followed by second-line E in advanced non-small cell lung cancer (aNSCLC): the TORCH trial. Program and abstracts of the 2010 Annual Meeting of the American Society of Clinical Oncology; June 4-8, 2010; Chicago, Illinois. Abstract 7508.

Background

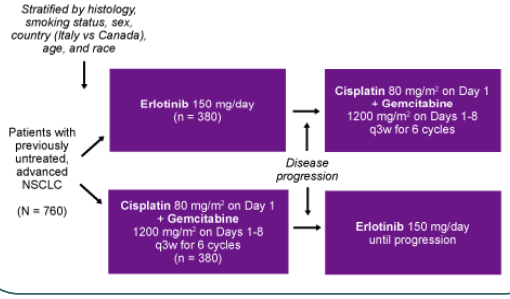
- Erlotinib in advanced NSCLC
  - Prolonged OS in pretreated, unselected patients with advanced NSCLC not eligible for further chemotherapy[2]
  - Phase II studies suggest erlotinib potential alternative to chemotherapy for first-line treatment in unselected patients[3,4]

2. Shepherd FA, Rodrigues Pereira J, Ciuleanu T, et al. Erlotinib in previously treated non-small-cell lung cancer. N Engl J Med. 2005;353:123-132.
3. Ciaccone G, Gallegos Ruiz M, Le Chevalier T, et al. Erlotinib for frontline treatment of advanced non-small cell lung cancer: a phase II study. Clin Cancer Res. 2006;12(20 Pt 1):6049-6055.
4. Jackman DM, Yeap BY, Lindeman NI, et al. Phase II clinical trial of chemotherapy-naive patients > or = 70 years of age treated with erlotinib for advanced non-small-cell lung cancer. J Clin Oncol. 2007;25:760-766.

TORCH: First-line Erlotinib Followed by Chemotherapy Inferior to First-line Chemotherapy Followed by Erlotinib in Advanced NSCLC

Current study assessed noninferiority in OS of first-line erlotinib followed with chemotherapy at disease progression vs first-line chemotherapy followed with erlotinib at disease progression

Schematic of Study Design



Eligibility

- Inclusion criteria
  - Cytologically or histologically confirmed NSCLC
    - Stage IIIB (with metastasis to supraclavicular nodes or with pleural effusion)
    - Stage IV
  - 18-70 years of age
    - Canadian centers did not apply upper age limit
  - ECOG performance score 0-1

Eligibility

- Exclusion criteria
  - Previous chemotherapy for advanced disease
    - Previous adjuvant treatment (> 1 year prior) permitted with no gemcitabine

Baseline Characteristics

Characteristic	Erlotinib → Chemotherapy (n = 380)	Chemotherapy → Erlotinib (n = 380)
Male, %	66	66
Age		
• Median age, yrs (range)	63 (27-79)	62 (34-81)
• Younger than 70 yrs of age, %	95	95
Country, %		
• Italy	81	81
• Canada	19	19
Race, %		
• East Asian	3	3
• Other	97	97
Smoking status, %		
• Never	21	21
• Former or current	79	79

Baseline Characteristics

Characteristic	Erlotinib → Chemotherapy (n = 380)	Chemotherapy → Erlotinib (n = 380)
ECOG performance score, %		
▪ 0	52	49
▪ 1	48	51
Stage, %		
▪ IIIB	12	10
▪ IV	88	90
Histology, %		
▪ Adenocarcinoma or BAC	55	56
▪ Other	45	44

BAC, bronchioloalveolar carcinoma.

Description of Current Analysis

- Primary endpoint
  - Overall survival (OS)

Description of Current Analysis

- Secondary endpoint
  - Toxicity
    - National Cancer Institute Common Terminology Criteria for Adverse Events v3
  - Response
    - Response evaluation criteria in solid tumors
  - PFS

Description of Current Analysis

- Secondary endpoint
  - Quality of life
    - European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 and LC13
  - Pharmacoeconomics
  - Biomarkers
    - Tumor
    - Blood

Main Findings

- First-line erlotinib inferior to first-line chemotherapy for OS in NSCLC

Median OS, mos	Erlotinib → Chemotherapy (n = 380)	Chemotherapy → Erlotinib (n = 380)	HR (95% CI)
Interim analysis*	7.7 (6.6-10.4)	10.9 (9.3-13.3)	1.40 (1.13-1.73)
Updated analysis†	8.5 (7.2-10.5)	12.0 (10.3-14.8)	1.36‡ (1.12-1.65)

*Cutoff November 2009; median follow-up: 8.3 months.
†Cutoff May 2010; median follow-up: 12.9 months.
‡$p = .002$

Main Findings

- Inferiority of first-line erlotinib for survival confirmed in subgroup analysis

HR of Death	HR	95% CI
Overall	1.36	1.12-1.65
Sex		
• Male	1.39	1.10-1.75
• Female	1.34	0.94-1.91
Histology		
• Adenocarcinoma or BAC	1.64	1.26-2.15
• Other*	1.09	0.82-1.45
Smoking status		
• Never	1.32	0.82-2.13
• Current/former	1.39	1.12-1.71

*Squamous cell carcinoma, large cell carcinoma, or undefined.

Main Findings

- Compared with chemotherapy, first-line erlotinib also had reduced responses as measured by other efficacy outcomes

Outcome	Erlotinib → Chemotherapy (n = 380)	Chemotherapy → Erlotinib (n = 380)
Median PFS,* mos (95% CI)	2.2 (2.1-2.4)	5.7 (4.9-6.4)
Objective response,† %	18	32
• CR with first-line treatment	< 1	1
• PR with first-line treatment	9	27
• CR with second-line treatment	1	< 1
• PR with second-line treatment	9	6
No response, %	82	68
• PD	27	17

*Assessment of first-line treatment only.
†ITT population.

Other outcomes

- Significantly higher toxicity in chemotherapy → erlotinib arm
- Only diarrhea and skin effects (including rash) higher in erlotinib → chemotherapy arm

Adverse Event (Any Grade),* %	Erlotinib → Chemotherapy (n = 380)	Chemotherapy → Erlotinib (n = 380)	P Value
Hematologic toxicity			
• Neutropenia	19	43	< .001
• Anemia	35	59	< .001
• Thrombocytopenia	15	33	< .001
Nonhematologic toxicity			
• Fatigue	56	65	.02
• Nausea	41	59	< .001
• Vomiting	22	41	< .001
• Constipation	19	29	< .001
• Neurotoxicity	20	27	.02

Other outcomes

Adverse Event (Any Grade),* %	Erlotinib → Chemotherapy (n = 380)	Chemotherapy → Erlotinib (n = 380)	P Value
• Hair loss	8	15	.004
• Renal toxicity	7	13	.003
• Allergy	2	4	.04
• Diarrhea	40	23	< .001
• Skin rash	68	34	< .001
• Other skin effect	40	21	< .001

*Reported with first-line or second-line treatment.

Summary of Key Conclusions

- First-line erlotinib followed by chemotherapy (cisplatin/gemcitabine) at progression
  - inferior to first-line chemotherapy followed by erlotinib at progression in unselected patients with advanced (stage IIIB/IV) non-small-cell lung cancer (NSCLC)
  - Lower efficacy outcomes
    - OS
    - PFS
    - ORR

Summary of Key Conclusions

- First-line chemotherapy followed by erlotinib at disease progression remains the standard of care for unselected patients with advanced stage NSCLC

Metastatic Melanoma

MDX010-20: multicenter, double-blind, randomized, placebo-controlled phase III trial[1]

1. O'Day S, Hodi FS, McDermott D, et al. A phase III, randomized, double-blind, multicenter study comparing monotherapy with ipilimumab or gp100 peptide vaccine and the combination in patients with previously treated, unresectable stage III or IV melanoma. Program and abstracts of the 2010 Annual Meeting of the American Society of Clinical Oncology; June 4-8, 2010; Chicago, Illinois. Abstract 4.

Background

- Metastatic melanoma associated with poor prognosis, rising incidence
  - Treatment options limited, with no therapies approved for previously treated patients
  - No treatments investigated in a randomized, placebo-controlled clinical trial have demonstrated survival benefit in this setting
- Two immunotherapeutic strategies demonstrated activity in earlier studies

Ipilimumab

- Fully human monoclonal antibody targeting CTLA-4, a receptor present on T-cell surface that normally downregulates T-cell activation

Ipilimumab

- Binding of ipilimumab to CTLA-4 promotes T-cell activation by antagonizing inhibitory activity of CTLA-4

Ipilimumab

- Associated with immune-associated adverse events
- Demonstrated durable responses as monotherapy in phase II study in patients with metastatic melanoma[2]

2. O'Day SJ, Maio M, Chiarion-Sileni V, et al. Efficacy and safety of ipilimumab monotherapy in patients with pretreated advanced melanoma: a multicenter single-arm phase II study. Ann Oncol. 2010;[Epub ahead of print].

gp100

- Vaccine restricted to patients expressing a specific major histocompatibility complex gene, *HLA-A*0201*

gp100

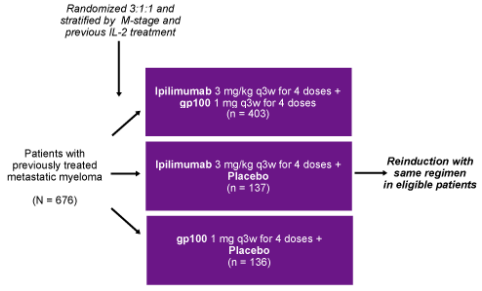
- Induces T-cell-specific immune responses
- Demonstrated activity in combination with interleukin-2 in patients with metastatic melanoma[3]

3. Schwartzentruber DJ, Lawson D, Richards J, et al. A phase III multi-institutional randomized study of immunization with the gp100:209-217(210M) peptide followed by high-dose IL-2 compared with high-dose IL-2 alone in patients with metastatic melanoma. Program and abstracts of the 2009 Annual Meeting of the American Society of Clinical Oncology; May 29 – June 2, 2009; Orlando, Florida. Abstract CRA9011.

Ipilimumab Improves Survival vs gp100 in Patients With Previously Treated Metastatic Melanoma

Current study compared efficacy, safety of ipilimumab, gp100, and a combination of both agents in patients with previously treated metastatic melanoma

Schematic of Study Design



Eligibility

- Main inclusion criteria
  - Previously treated stage III or IV melanoma
  - *HLA-A*0201* positive
  - Previously treated central nervous system metastases permitted
  - No exclusions based on lactate dehydrogenase (LDH) level

Eligibility

- Exclusion criteria
  - Autoimmune disease
  - Previous therapy with anti–CTLA-4 antibody
  - Previous therapy with anticancer vaccine

Baseline Characteristics

Characteristic	Ipilimumab + gp100 (n = 403)	Ipilimumab + Placebo (n = 137)	gp100 + Placebo (n = 136)
Mean age, yrs	55.6	56.8	57.4
Male, %	61	59	54
M stage, %			
• M0-M1a	10	11	11
• M1b	19	16	17
• M1c	71	73	72
ECOG performance score			
• 0	58	53	52
• 1	41	47	45
• 2-3	1.2	0.7	3
LDH > ULN, %	37	39	38
CNS metastases, %	11	11	15

Description of Current Analysis

- Patients recruited from September 2004 - July 2008 from 125 centers in 13 countries

Description of Current Analysis

- Primary endpoint
  - In January 2009 (prior to unblinding) changed from best ORR to OS
  - Primary comparison: ipilimumab plus gp100 vs gp100
    - 90% power to detect OS increase from 8.6 to 10.8 months with 385 events
  - Secondary comparison: ipilimumab vs gp100
    - 80% power to detect 2-month increase in OS with 219 events

Description of Current Analysis

- Secondary endpoint
  - Best ORR
  - Safety

Main Findings

- Ipilimumab associated with significant OS benefit vs gp100, whether used in combination with gp100 or as monotherapy

OS Outcome	Ipilimumab + gp100 (n = 403)	Ipilimumab + Placebo (n = 137)	gp100 + Placebo (n = 136)
Median OS, mos	10.0	10.1	6.4
1-yr OS, %	44	46	25
2-yr OS, %	22	24	14

Main Findings

- Superior PFS with ipilimumab vs gp100, ipilimumab vs combination therapy

PFS Comparison	HR	95% CI	P Value
Ipilimumab + gp100 vs gp100	0.81	0.66-1.00	.0464
Ipilimumab vs gp100	0.64	0.50-0.83	.0007
Ipilimumab + gp100 vs ipilimumab	1.25	1.01-1.53	.0371

Main Findings

- Superior response rates, disease control rates with ipilimumab-containing regimens vs gp100 alone

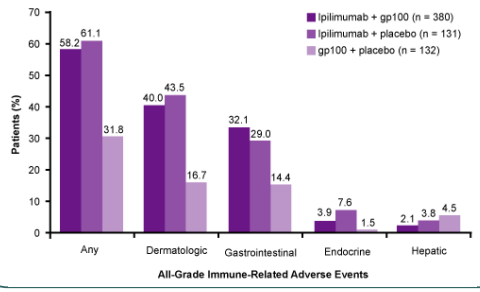
Outcome	Ipilimumab + gp100 (n = 403)	Ipilimumab + Placebo (n = 137)	gp100 + Placebo (n = 136)	P Value (Ipilimumab + gp100 vs gp100)	P Value (Ipilimumab vs gp100)
Best ORR, %	5.7	10.9	1.5	.0433	.0012
Disease control rate (CR + PR + SD), %	20.1	28.5	11.0	.0179	.0002

Other outcomes

- Ipilimumab associated with higher rate of grade 3/4 treatment-related adverse events

Treatment-Related Adverse Event, %	Ipilimumab + gp100 (n = 380)	Ipilimumab + Placebo (n = 131)	gp100 + Placebo (n = 132)
Any	88.9	80.2	78.8
Grade 3/4	17.4	22.9	11.4
Death	2.1	3.1	1.5

High incidence of immune-related adverse events in ipilimumab arms



High incidence of immune-related adverse events in ipilimumab arms

- Grade 1/2 events generally reversible
- Incidence of immune-related grade 3/4 events with ipilimumab: 10% to 15%
- Can usually be treated with steroids
- Incidence of immune-related deaths with ipilimumab: 1.3% to 1.5%

Summary of Key Conclusions

- Ipilimumab, a anticytotoxic T-lymphocyte antigen-4 (CTLA-4) monoclonal antibody, associated with significant increase in OS, PFS, and response rates vs gp100 peptide vaccine in patients with previously treated metastatic melanoma
  - Represents first randomized phase III trial to demonstrate survival benefit in metastatic melanoma

Summary of Key Conclusions

- No OS or PFS benefit with addition of gp100 to ipilimumab
- Ipilimumab associated with increased rate of grade 3/4 treatment-related adverse events related to its immunomodulatory mechanism of action
- Can be managed with high-dose steroids in majority of patients

Pancreatic Cancer

Randomized phase III trial comparing FOLFIRINOX (F: 5FU/leucovorin [LV], irinotecan [I], and oxaliplatin [O]) versus gemcitabine (G) as first-line treatment for metastatic pancreatic adenocarcinoma (MPA): Preplanned interim analysis results of the PRODIGE 4/ACCORD 11 trial.

Conroy T, et al. J Clin Oncol 28:15s, 2010 (suppl; abstr 4010)

Background

- Gemcitabine has been considered the standard systemic therapy for unresectable pancreatic cancer since the late 1990s
  - Gemcitabine derived significantly more clinical benefit than those receiving 5-FU (23.8% vs 4.8%, respectively; *P* = .0022).

Background

Study, Yr	N	Regimen	ORR	Median OS, mos	1-Yr OS, %
Burris et al, 1997[5]	126	Gem vs 5-FU	23.8 4.8	5.65 4.41	18 2
Bramhall et al, 2001[11]	414	Gem vs marimastat (3 dose levels)	--	5.57 3.50-4.10	19 14-20
Bramhall et al, 2002[12]	239	Gem vs gem/marimastat	16.0 11.0	5.50 5.50	17 18
Moore et al, 2003[13]	277	Gem vs BAY 12-9566	5.9 2.96	6.59 3.74	25 10
Moore et al, 2007[14]	569	Gem vs gem/erlotinib	8.0 8.6	5.91 6.24*	23 17
Kindler et al, 2007[15]	602	Gem vs gem/bevacizumab	47.0 54.0	5.70 6.00	~ 18 ~ 18
Philip et al, 2007[16]	735	Gem vs gem/cetuximab	14 12	5.9 6.4	NR

CALGB, Cancer and Leukemia Group B; Gem, gemcitabine; ORR, overall response rate; OS, overall survival.
**P = .038*

Background

- In a phase II trial of Folfirinox (F) in 35 metastatic pancreatic cancer
  - 26% response rate
  - Median survival of 9.5 months (mo)
  - Quality of life improvement

Conroy, JCO 2005

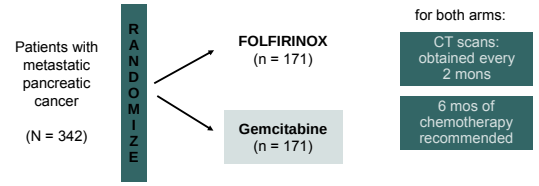
Background

- In a randomized phase II trial of F vs G in 88 MPA patients (pts),
  - F induces a response rate > 30%

F (O 85 mg/m^2 d1 + I 180 mg/m^2 d1 + LV 400 mg/m^2 d1 followed by 5FU 400 mg/m^2 bolus d1 and 2,400 mg/m^2 46h continuous infusion biweekly) or G (1g/m^2 IV weekly x7, 1 w rest, then weekly x 3q4w).

Ychou, ASCO 2007

PRODIGE 4/ACCORD 11 Trial Design

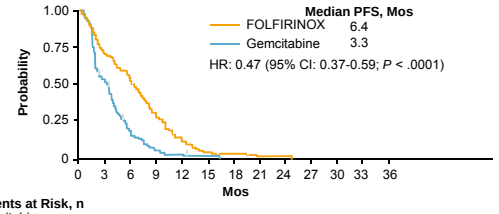


Stratified by

- Center
- Performance score 0 vs 1
- Location of the tumor: head vs other location of the primary

Conroy T, et al. ASCO 2010. Abstract 4010. Reprinted with permission.

PRODIGE 4/ACCORD 11: Progression-Free Survival

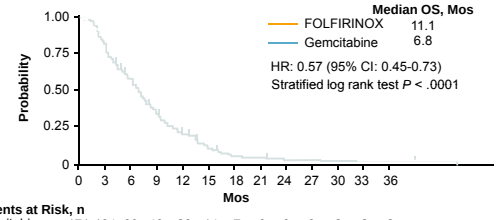


Patients at Risk, n

Gemcitabine	171	88	26	8	5	2	0	0	0
FOLFIRINOX	171	121	85	42	17	7	4	1	1

Conroy T, et al. ASCO 2010. Abstract 4010. Reprinted with permission.

PRODIGE 4/ACCORD 11: Overall Survival



Patients at Risk, n

Gemcitabine	171	134	89	48	28	14	7	6	3	3	2	2	2
FOLFIRINOX	171	146	116	81	62	34	20	13	9	5	3	2	2

Conroy T, et al. ASCO 2010. Abstract 4010. Reprinted with permission.

PRODIGE 4/ACCORD 11: Safety

Select Grade 3/4 Adverse Events, %	FOLFIRINOX (n = 167)	Gemcitabine (n = 167)	*P* Value
Neutropenia	45.7	18.7	.0001
Febrile neutropenia	5.4	0.6	.009
Thrombocytopenia	9.1	2.4	.008
Anemia	7.8	5.4	NS
Peripheral neuropathy	9.0	0	.0001
Vomiting	14.5	4.7	.002
Fatigue	23.2	14.2	.036
Diarrhea	12.7	1.2	.0001
ALT	7.3	18.6	.0022

Conroy T, et al. ASCO 2010. Abstract 4010.

PRODIGE 4/ACCORD 11: Conclusions

- In patients with metastatic pancreatic cancer FOLFIRINOX associated with significant improvements in PFS and OS vs gemcitabine
  - Median OS: 11.1 mos; reduced risk of disease progression by 53%
- FOLFIRINOX associated with significantly increased incidence of adverse events, although significantly (*P* = .001) delays QoL degradation vs gemcitabine
- Investigators asserted that FOLFIRINOX potential new standard of care in this setting

McCahill LE, et al. ASCO 2010. Abstract 3527.

Summary

- PRODIGE 4/ACCORD 11: FOLFIRINOX associated with significant improvements in PFS, OS and increased incidence of AEs vs gemcitabine as first-line treatment for metastatic pancreatic cancer

Other GI cancers

- CRYSTAL/OPUS pooled analysis: cetuximab plus chemotherapy associated with significant improvements in OS, PFS, and response rate in patients with mCRC and *KRAS* wild-type tumors
  - *BRAF* mutation not predictive of response to cetuximab plus chemotherapy, but is prognostic of poor survival outcome
- COIN: no improvement in OS or PFS with addition of cetuximab to oxaliplatin-based chemotherapy previously untreated advanced CRC
  - *KRAS*, *BRAF*, and *NRAS* mutation status strongly prognostic; those with mutated *BRAF* had poorest prognosis

Other GI cancers (cont)

- N0147: adjuvant mFOLFOX + cetuximab does not improve rates of DFS, OS in resected stage III colon cancer vs mFOLFOX
- MACRO: after bevacizumab + XELOX induction therapy for patients with mCRC, maintenance bevacizumab comparable to continued bevacizumab + XELOX
- PRIME: in patients with mCRC, first-line panitumumab + FOLFOX4 associated with significantly improved PFS in patients with *KRAS* wild-type tumors, significantly worse PFS in patients with *KRAS*-mutated tumors vs FOLFOX4
  - Grade 2-4 skin toxicity associated with significantly longer PFS and OS vs grade 0/1 skin toxicity, regardless of *KRAS* mutation status

Summary

- NASBP Protocol C10: in patients with stage IV CRC and asymptomatic primary tumors receiving mFOLFOX6 plus Bev without resection, low rate of primary events suggests these patients can be spared initial noncurative resection of primary tumor
- Phase II randomized comparison of modified DCF vs DCF demonstrated comparable OS and time to treatment failure in metastatic gastric cancer
  - Modified DCF had improved toxicity profile vs DCF + G-CSF