FOLFIRINOX - Oxaliplatin 85 / Folinic Acid 400 / Irinotecan 180 / Fluorouracil 2400, Pancreatic Cancer

Protocol-ID: 47 V1.4 (Complete), FOLFIRINOX (OXAL85/CFOL400/IRIN180/FU2400), Pankreas-Ca

Indication(s)

- Pancreatic Cancer; ICD-10 C25.-

Protocol classification

- Classification: current standard
- Intensity: Standard dose
- Therapy mode: First line
- Therapy intention: palliative

Cycles

Cycle length 14 days, recommended cycles: 12

Risks

- Emetogenicity (MASCC/ESMO): moderate (30-90%)
- Neutropenia: very high (>41%) Grade 3 and 4; 42.5% with G-CSF
- Febrile Neutropenia: intermediate (10-20%) Grade 3 and 4; 1 death, 42.5% with G-CSF
- Thrombocytopenia below 50 000/µl: low (<10%)
- Anemia Hb below 8g/dl: moderate (6-15%)
- Diarrhea: CTC AE °3-4: 12.7%
- Fatigue: CTC AE °3-4: 23.6%
- Vomiting: CTC AE °3-4: 14.5%
- Thromboembolic Event: CTC AE °3-4: 6.6%
- Neuropathy: CTC AE °3-4: 9.0%
- Increase Aminotransferases: CTC AE °3-4: 7.3%

Therapy

Hydration: Balanced Crystalloid Solution **HYD**

Access: peripheral venous

Hydration before, during, or after antitumor therapy

Day	Substance	Dosage	Solution	Appl.	Inf. time	Procedure
1	**Balanced Crystalloid Solution**	500 ml		i.v.	60 min	60 min before Oxaliplatin (d1)

Antiemesis: Emetogenicity moderate, GRAN i.v., DEXA i.v. **AE**

Access: peripheral venous

ASCO 2015, DGHO 2016, DKG 2016, MASCC/ESMO 2016, if palonosetron not available

Day	Substance	Dosage	Solution	Appl.	Inf. time	Procedure
1	**Dexamethasone**	8 mg	NaCl 0.9% 50 ml	i.v.	5 min	30 min before Oxaliplatin (d1)
1	**Granisetron**	1 mg	NaCl 0.9% 50 ml	i.v.	5 min	15 min before Oxaliplatin (d1)
or other 5-HT3 antagonist						
2-3	**Dexamethasone**	8 mg		p.o.		1-0-0-0

Antineoplastic therapy: FolFIrinOx **CTX**

Access: central venous

5-FU, folinic acid, irinotecan, and oxaliplatin in pancreatic cancer

Day	Substance	Dosage	Solution	Appl.	Inf. time	Procedure
1	**Oxaliplatin**	85 mg/m² BSA	Dextrose 5% 500 ml	i.v.	2 h	Sequence
1	**Folinic acid**	400 mg/m² BSA	NaCl 0.9% 250 ml	i.v.	2 h	Sequence
1	**Irinotecan**	180 mg/m² BSA	NaCl 0.9% 250 ml	i.v.	90 min	90 min before Fluorouracil (d1)
Irinotecan is administered 30 minutes after the start of the folinic acid infusion in parallel with folinic acid.						
1	**Fluorouracil**	400 mg/m² BSA	none	i.v.	1 min	Sequence
Bolus application						
1	**Fluorouracil**	2400 mg/m² BSA	NaCl 0.9% 500 ml	i.v.	46 h	Sequence
The volume of the carrier solution refers to inpatient therapy with infusion pumps. When using syringe pumps or ambulatory systems, a different volume (e.g. 100 ml) can be used.						

Hematopoietic growth factors: FN risk 10-20%, G-CSF long-acting, pegylated **HW**

Access: - none -

Risk of febrile neutropenia (FN) 10-20% and 1 risk factor: age > 65 y, laboratory parameters (anemia, lymphocytopenia < 700/µl, hypalbuminemia, hyperbilirubinemia) previous chemotherapy, comorbidities, low performance status, advanced symptomatic tumor disease (DKG 2016)

Day	Substance	Dosage	Solution	Appl.	Inf. time	Procedure
4	**Pegfilgrastim**	6 mg		subc	Bolus	24 h after Fluorouracil (d1)
Use at risk: FN 10-20% and 1 risk factor, other long-acting G-CSF possible.						

Substance links

Links to substances are found here.

Concomitant therapy supplements

If a cholinergic syndrome occurs during Irinotecan, according to the summary of product characteristics, 0.25 mg Atropine sulphate should be administered subcentrally; if a history of cholinergic syndrome is known, Atropine should be administered prophylactically before Irinotecan.
Loperamide can be used to treat the onset of delayed diarrhea.

Notes

Increase the risk of febrile neutropenia to medium, as one death due to febrile neutropenia occurred in the study. Filgrastim application was required in 42.5% of patients.
For patients with a response, 6 months of therapy was recommended in the literature.

Cycle diagram

Hydration: Balanced Crystalloid Solution

	Week 1 / d						
Substance	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Balanced Crystalloid Solution (i.v.)	■						

Antiemesis: Emetogenicity moderate, GRAN i.v., DEXA i.v.

	Week 1 / d						
Substance	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Dexamethasone (i.v.)	■						
Granisetron (i.v.)	■						
Dexamethasone (p.o.)		■	■				

Antineoplastic therapy: FolFIrinOx

	Week 1 / d						
Substance	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Oxaliplatin (i.v.)	■						
Folinic acid (i.v.)	■						
Irinotecan (i.v.)	■						
Fluorouracil (i.v.)	■						
Fluorouracil (i.v.)	■						

Hematopoietic growth factors: FN risk 10-20%, G-CSF long-acting, pegylated

	Week 1 / d						
Substance	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Pegfilgrastim (subc)				■			

Cycles

Cycle length 14 days, recommended cycles: 12

Controls:

- Blood count: on day 1 and subsequently weekly
- DPD Exclude deficiency: Uracil levels or DPD gene mutations.
- Day 1: Anamnesis and clin. examination regarding neuropathy
- Day 1: GOT, GPT, GGT, Bilirubin, AP, Cholinesterase Irinotecan: increased risk of toxicity due to decreased hepatic clearance with elevated bilirubin between 1.5 and 3 times the norm, see summary of product characteristics for dose adjustment. Do not administer if bilirubin > 3 times normal elevated. Regular blood count and bilirubin checks in hepatic insufficiency. Fluorouracil: liver monitoring during therapy. Severe hepatic insufficiency is a contraindication.
- Day 1: Creatinine, glomerular filtration rate (GFR) Oxaliplatin: no use in patients with severe renal impairment creatinine clearance < 30 ml/min. Irinotecan: no studies on renal insufficiency, use in renal insufficiency is therefore not recommended. Fluorouracil: control of retention values

Dose adjustment

- **Fluorouracil**
  - **for Bone Marrow Insufficiency**: **Platelets**
    >100,000 T./µl- 100% dose; 70000-100000 T./µl- 75% dose; 50000-70000 T./µl- 50% dose; <50000 T/µl STOP!
  - **for Bone Marrow Insufficiency**: **Leukocytes**
    >4000 L./µl- 100% dose; 3000-4000 L./µl- 75% dose; 2000-3000 L./µl- 50% dose; <2000 L./µl STOP!
- **Oxaliplatin**
  - **for Renal Failure**: **Glomerular Filtration Rate (GFR)**
    No data on patients with severe renal impairment (contraindication if creatinine CL < 30ml/min). In moderate renal impairment, close monitoring and dose adjustment according to toxicity. In case of mild renal impairment no dose adjustment necessary
  - **for Bone Marrow Insufficiency**: **Neutrophils**
    In case of neutrophil count< 1500/µl, the next treatment cycle must be postponed until acceptable values are reached. Before starting oxaliplatin treatment and each new cycle, a complete blood count including differential white blood cell count is required.
  - **for Bone Marrow Insufficiency**: **Platelets**

If the platelet count is <50000/µl, the next treatment cycle must be postponed until acceptable values are reached. Prior to initiation of oxaliplatin treatment and each new cycle, a complete blood count including white blood cell differential must be performed.

Original indication

Pancreatic carcinoma (adeno-), metastatic, ECOG 0-1

Original author

Conroy, Thierry (2011)

Origin

Groupe Tumeurs Digestives of Unicancer and the PRODIGE Intergroup

References

- Conroy T, FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer.; N Engl J Med 2011 May 12;364(19):1817-25. doi: 10.1056/NEJMoa1011923. PMID: 21561347. [PMID]
- Conroy T, Irinotecan Plus Oxaliplatin and Leucovorin-Modulated Fluorouracil in Advanced Pancreatic Cancer, A Groupe Tumeurs Digestives of the Fédération Nationale des Centres de Lutte Contre le Cancer Study; J Clin Oncol 2005 Feb 20;23(6):1228-36. doi: 10.1200/JCO.2005.06.050. PMID: 15718320. [PMID]
- Ducreux M, Cancer of the pancreas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2015 Sep;26 Suppl 5:v56-68. doi: 10.1093/annonc/mdv295. PMID: 26314780. [PMID]

Recommendations

- 11/2023: European Society for Medical Oncology
- 06/2023: National Comprehensive Cancer Network

Status

Valid since 2024-09-20, Version 1.4, last updated 2024-09-17

Last modification: V1.4: Correction of relative times and days Pegfilgrastim. V1.3: Correction title, correction antiemesis V1.2: New Cato import due to cycle counting and diagnosis assignment by ICD-10 codes. V1.1: Cato test done. V1.0: Run times and substance sequence according to primary literature.

Important notice