

NEN PRECEPTORSHIP LA PRATICA CLINICA NELLE NEOPLASIE NEUROENDOCRINE

5/6 Aprile 2018

IEO, Istituto Europeo di Oncologia - Milano

TRIAL CLINICI

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Studi clinici aperti all'arruolamento

<u>Lung</u>	<u>ATLANT</u> (phase II) Lanreotide + temozolomide in with progressive well differentiated thoracic NEN
<u>High grade</u> <u>(Ki-67 21-55%)</u> <u>GEP and lung NEN</u>	<u>MAVERIC</u> (spontaneous study) Everolimus as maintenance
<u>GEP (gastro- entero- pancreatic) NEN</u>	<u>RADIONET</u> identification of NET node metastases

Studi clinici di imminente apertura

<u>GI NET</u>	→ ✓ <u>PDR001</u> (phase II) efficacy and safety of PDR001 ✓ <u>ROBONET</u> robotic surgery and fluorescence n SI- NETs → ✓ <u>SSA +/- Axitinib</u>
<u>Pancreatic NET</u>	✓ <u>COMPETE</u> (phase III) - PRRT vs EVE ✓ <u>Preoperative PRRT (phase II)</u> PRRT -> surgery vs surgery upfront ✓ <u>ENETS ASPEN trial</u> Pan-NETs <2 cm of diameter →
<u>LUNG NET</u>	→ ✓ <u>PDR001</u> → ✓ <u>SSA +/- Axitinib</u>
<u>Poorly differentiated</u>	→ ✓ <u>PDR001</u>

Studi clinici con arruolamento chiuso ma con pazienti in trattamento

<u>Pancreas</u>	<u>IEO 695</u> (phase IV) - sunitinib in advanced or metastatic PanNET <u>ROLLOVER</u> everolimus roll-over protocol <u>TALENT</u> (phase II) - Lenvatinib <u>PDR001</u>    <u>IEO 694 - Radiant 4</u>
<u>GEP NEN</u>	<u>TALENT</u> <u>PDR001</u>    <u>IEO 694 - Radiant 4</u>
<u>Lung</u>	  <u>PDR001</u> <u>IEO 694 - Radiant 4</u> <u>LUNA</u> Pasireotide LAR or Everolimus alone or in combination

Studi clinici carcinoma a cellule di Merkel

IEO 620 - Javelin Merkel	Avelumab in not-pretreated patients with Merkel cell carcinoma (MCC)
Avelumab Early Access – Single Patient Use	Avelumab in pretreated patients with MCC

New patients..

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TROVA UN MEDICO PRENOTA UNA VISITA RAGGIUNGICI CONTATTACI SOSTIENI IEO

CHI SIAMO PER I PAZIENTI PREVENZIONE RICERCA FORMAZIONE SCIENCE IN SOCIETY

Un istituto di riferimento dove la ricerca sui tumori diventa cura in tempo reale

News

Ultime notizie dallo IEO

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We updated the design of this site on December 18, 2017. [Learn more.](#)

NIH U.S. National Library of Medicine

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ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world.

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Before participating in a study, talk to your health care provider and learn about the [risks and potential benefits](#).

Find a study (all fields optional)

Recruitment status ⓘ

☐ Recruiting and not yet recruiting studies

☐ All studies

Condition or disease ⓘ (For example: breast cancer)

X

Other terms ⓘ (For example: NCT number, drug name, investigator name)

X

Country ⓘ

X

[Search](#) [Advanced Search](#)

endocrini

LIGHT

di riferimento per la pratica
ricerca della Divisione sono quelle
regionali (ROL: Rete Oncologica
nazionali (AIOM, ItaNET),
(ESMO, ASCO, ENETS,

Team della Divisione di Oncologia Medica Gastrointestinale e Tumori Neuroendocrini

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Cella Chiara Alessandra
Rubino Manila
Pellicori Stefania
Laffi Alice
Pozzari Marta

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Mazzon Cristina

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Segretaria: Italia Paola



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Un istituto di riferimento dove la ricerca sui tumori diventa cura in tempo reale

IL NOSTRO STAFF

ONCOLOGIA MEDICA GASTROINTESTINALE E TUMORI NEUROENDOCRINI

Direttore
NICOLA FAZIO

STAFF ONCOLOGIA MEDICA GASTROINTESTINALE E TUMORI NEUROENDOCRINI

Medico con incarico di alta specializzazione Maria Giulia Zampino	Medico Stefania Pellicori	Medico Maria Saveria Rotundo
Medico Chiara Alessandra Cella	Medico Paola Simona Ravenda	Medico Francesca Spada

AGENDA

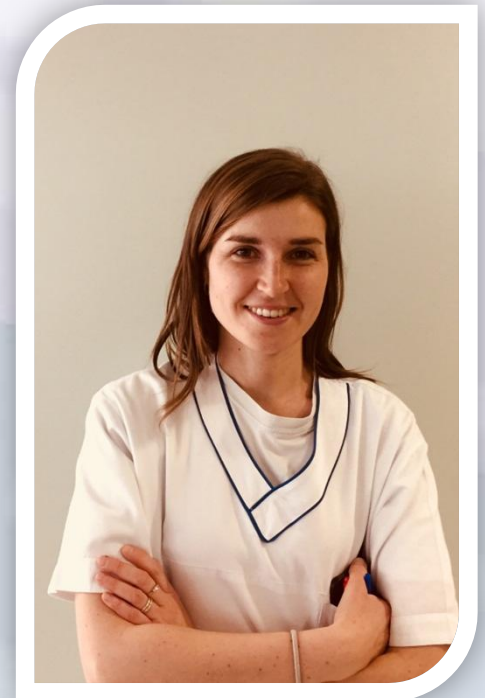
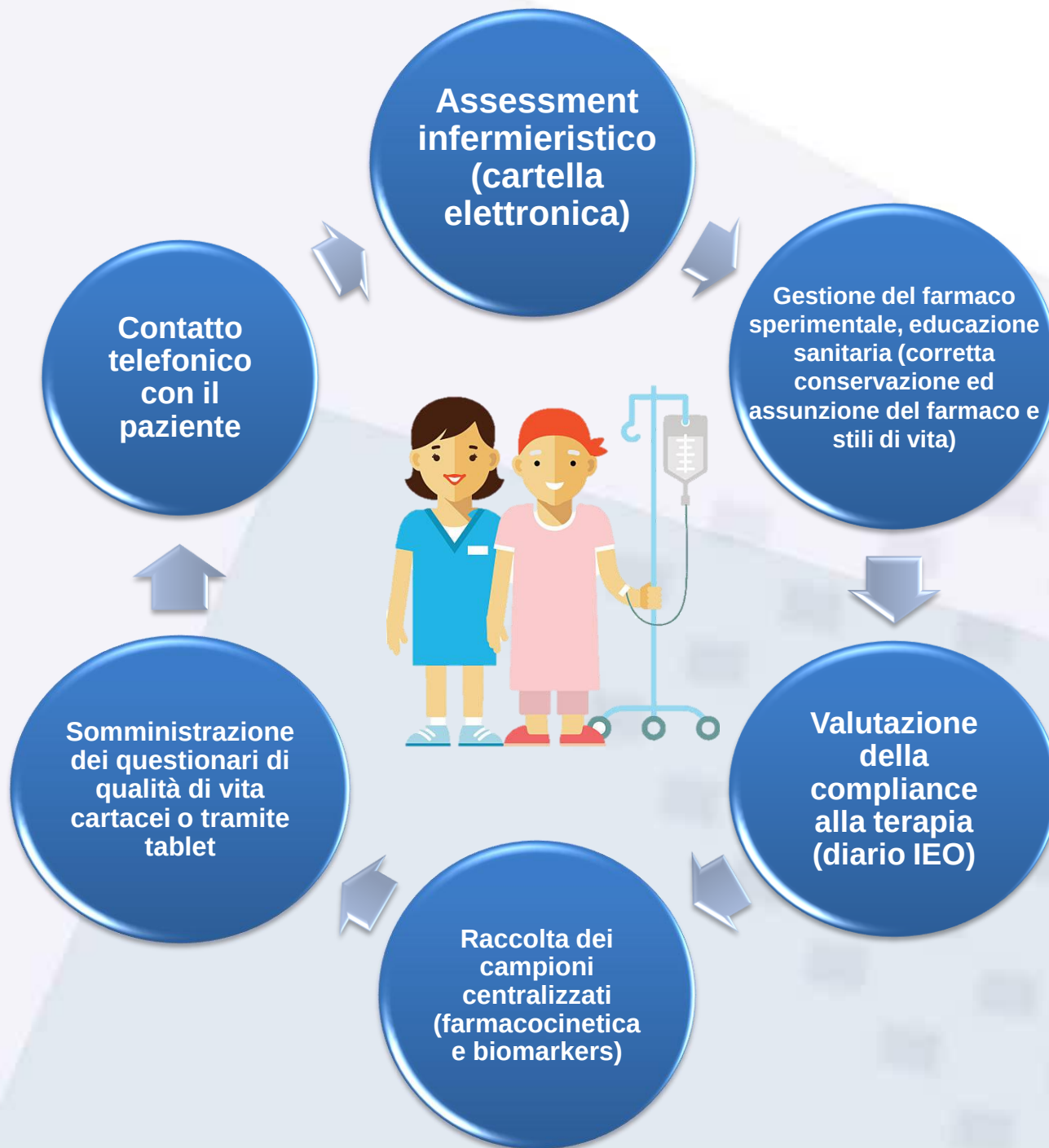
-  **LUNEDÌ → DISCUSSIONE CASI PAZIENTI IN TRIAL**
-  **MARTEDÌ → DISCUSSIONE MULTIDISCIPLINARE CASI CLINICI NET**
-  **MERCOLEDÌ → DH OMG NET**
-  **GIOVEDÌ → AMBULATORIO SSN NET E VISITE MULTIDISCIPLINARI**
-  **VENERDÌ → DISCUSSIONE CASI CLINICI E DH OMG**

Coordinatori di Ricerca Clinica



Infermiera di ricerca

IEO
Istituto Europeo di Oncologia



patients and clinical trials



first visit

Screening visit

LIST EXAMS

- ☒ **MEDICAL HISTORY**
- ☒ **WRITTEN INFORMED CONSENT**
- ☒ **PHYSICAL EXAMINATION**
- ☒ **LABORATORY EXAMINATION**
- ☒ **TUMOR EVALUATION (IMAGING, MAPPING OF SKIN LESIONS)**
- ☒ **CARDIOLOGICAL VISIT**
- ☒ **INCLUSION / EXCLUSION CRITERIA**

Selection of Trial Population

5.3

5.3.1

Inclusion Criteria

For inclusion in the trial, all of the following inclusion criteria must be met:

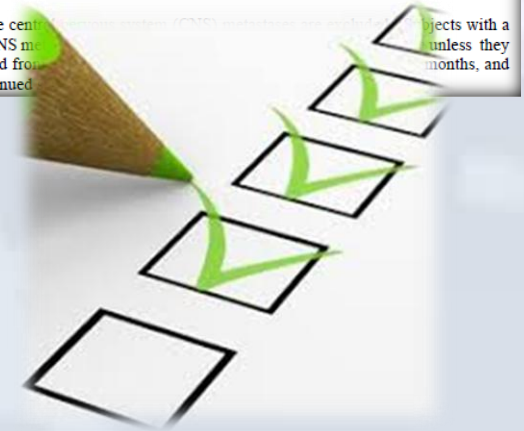
1. Signed written informed consent
2. Male or female subjects aged ≥ 18 years
3. Histologically proven MCC
 - a. Confirmation of the diagnosis by immunohistochemistry and/or appropriate cytokeratin expression (laboratory testing) in the tumor
 - b. Subjects must have metastatic disease that is recurrent or unresectable and not amenable to curative resection
 - c. For Part A: Subjects must have received prior systemic therapy for metastatic MCC that was administered. Subjects must not have received prior chemotherapy regimens for metastatic MCC including topotecan, doxorubicine, epirubicin, or combination with carboplatin
 - d. For Part B: Subjects must not have received prior systemic therapy for metastatic MCC. Prior chemotherapy for metastatic disease; no metastatic disease within 6 months prior to study start

Exclusion Criteria

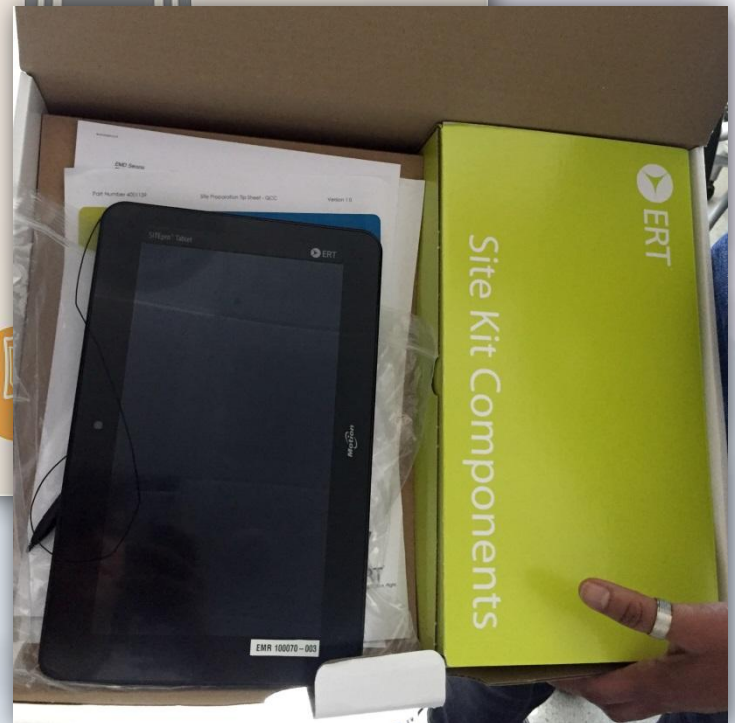
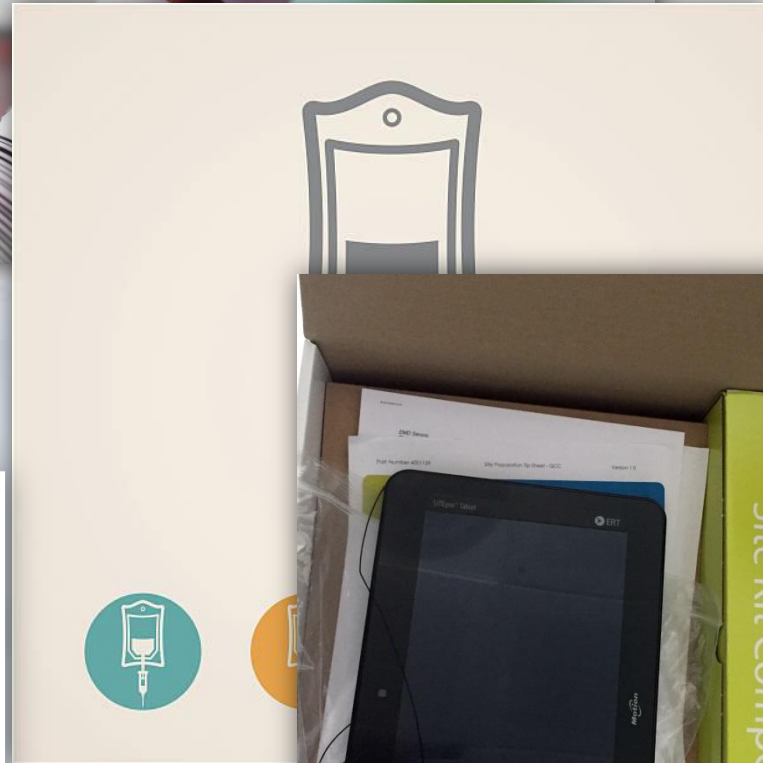
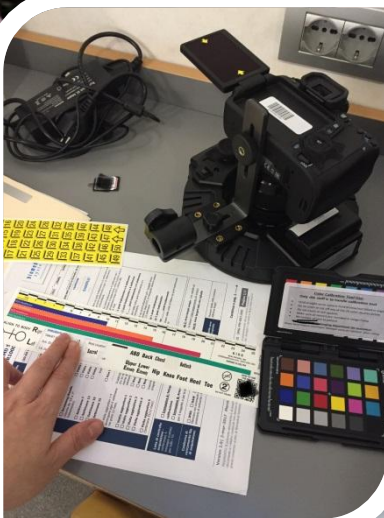
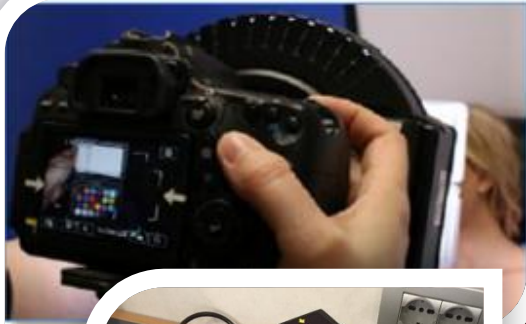
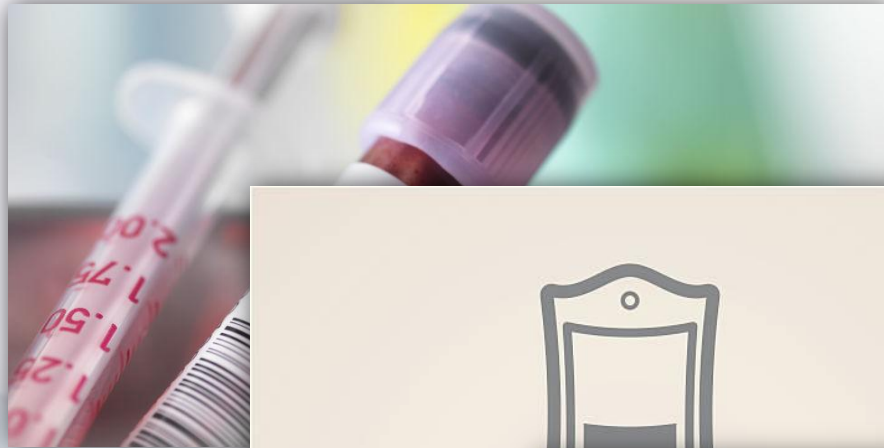
5.3.2

Subjects are not eligible for this trial if they fulfill any of the following exclusion criteria:

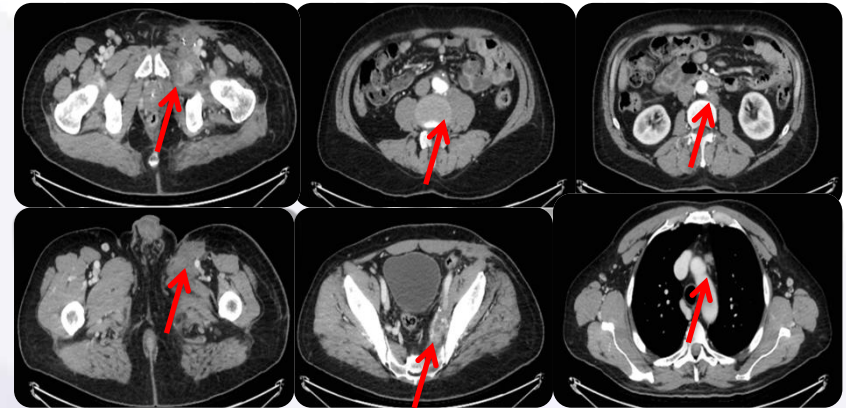
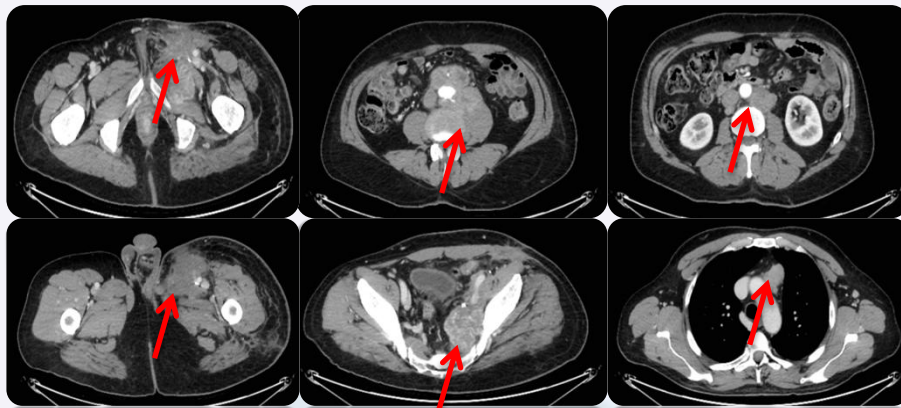
1. Participation in another interventional clinical trial within the past 30 days (participation in observational studies are permitted)
2. Concurrent treatment with a nonpermitted drug
3. Prior therapy with any antibody/drug targeting T-cell coregulatory proteins (immune checkpoints) such as anti-PD-1, anti-PD-L1, or anticytotoxic T-lymphocyte antigen-4 (CTLA-4) antibody; for Part B, the Investigator must consult with the Medical Monitor and consider other co-regulatory targets such as 4-1BB
4. Concurrent anticancer treatment (for example, cytoreductive therapy, radiotherapy [with the exception of palliative bone-directed radiotherapy, or radiotherapy administered on non-target superficial lesions], immune therapy, or cytokine therapy except for erythropoietin). Radiotherapy administered to superficial lesions is not allowed if such lesions are considered target lesions in the efficacy evaluation or may influence the efficacy evaluation of the investigational agent
5. Major surgery for any reason, except diagnostic biopsy, within 4 weeks and/or if the subject has not fully recovered from the surgery within 4 weeks
6. Concurrent systemic therapy with steroids or other immunosuppressive agents, or use of any investigational drug within 28 days before the start of trial treatment. Short-term administration of systemic steroids (that is, for allergic reactions or the management of irAEs) is allowed while on study. Note: Subjects receiving bisphosphonate or denosumab are eligible
7. Subjects with active central nervous system (CNS) metastases are eligible for the trial unless they have fully recovered from the CNS metastases within 6 months, and do not require continued treatment



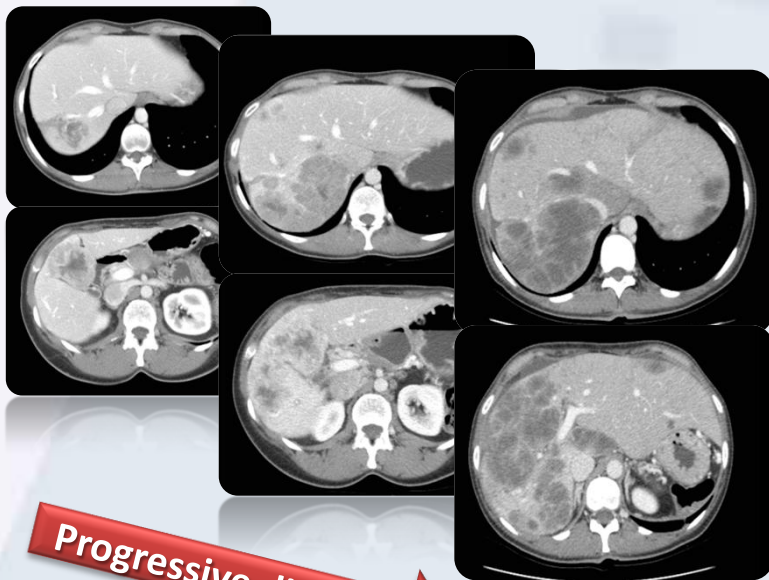
First day of treatment



Assessment during the treatment



partial response



Progressive disease



irRECIST	RECIST 1.1
Unidimensional	Unidimensional
≥ 10 mm	≥ 10 mm
5 lesions total, 2 per organ	5 lesions total, 2 per organ
Incorporated into TTB	Always represents PD
CR = disappearance of all lesions	CR = disappearance of all lesions
PR $\geq 30\%$ decrease from baseline TTB	PR $\geq 30\%$ decrease from baseline TTB
SD = when neither PR nor PD can be established	SD = when neither PR nor PD can be established
PD $\geq 20\%$ increase in the nadir of TTB (minimum 5 mm)	PD $\geq 20\%$ increase in the nadir of TTB (minimum 5 mm)
Yes, wait up to 12 weeks to confirm PD to account for flare	Yes, if response is primary endpoint

CRF (case report form)

lxa49196 - Case Report Forms - 3060001/XXX

Subject: 3060001/XXX

Home Enroll Subjects Queries Signatures Reports Documents Admin

CONSENT SCREENING CUMUL EVAL UNCOH W1D1b W3D15b W5D29b W7D43b W9D57b W11D71b EVALum RBAS W1D1a W3D15a W5D29a W7D43a W9D57a W11D71a W13D85a W15D99a W17D113a W19D127a W21D141a W23D155a W25D169a ADDITIONAL DISC EOT SPUR LPUP EASSV STERM DTH

Visit: DISEASE HISTORY

SCREENING

Forms: dov dem dishist qol mhx mhxdt prothr pmradio sphar sphardt thioop brain pe vs1 ecog ecg hema hemo chem lab urin1 micro preg1 sero horm her2 sentry rescr end

1.* Site of primary tumor (ICD-O) ☒ Stomach adenocarcinoma ☐ Gastro-esophageal junction adenocarcinoma

2.* Sub Sites ☐ Proximal ☐ Distal

3.* Tumor histopathology

4.* Date of Initial Cancer

5.* TNM classification

6.* TNM classification

7.* Date of documents

Other molecular abnormalities

8.* Record identifier

Note: Proximal -> upper Distal -> lower site

MO29112 - Irccs Istituto Europeo Di Oncologia Ieo On. 4761 Screening Visit RECIST 1.1 - Tumor Assessment - Target Les...

Date subject signed general consent for study participation (dd MMM/yyyy) 08 JUL 2015 Cohort: Cohort 2

Subject: 4761 Page: RECIST 1.1 - Tumor Assessment - Target Lesions (Screening) - Screening Visit

Exam/scan date (dd MMM/yyyy) 15 JUL 2015

CT slice thickness 5 mm

CT slice thickness unit MM

MRI slice interval mm

MRI slice interval unit MM

Colorectal cancer history

Smoking History

Alcohol Use History

Drug Abuse History

Vital Signs (Screening)

ECOG Performance Status

Physical Examination

Lab - Hematology

Lab - Coagulation

Lab - Blood chemistry

Lab - Blood chemistry

Lab - Urinalysis

Archival tumour tissue

RECIST 1.1 - Tumor Assessment - Target Lesions (Screening)

RECIST 1.1 - Tumor Assessment - Non-Target Lesions Assessment (Screening)

RECIST 1.1 - Tumor Assessment - Non-Target Lesions (Screening)

Protocol Amendment

Navigation

Change Site > 0900 > 1137-0900-205 > Study Level Forms > Adverse Events > 21 anemia 31 MAY 2017

Printable Version View PDF Icon Key CRF Version 3074 - Page Generated: 10 Mar 2017

4 alopecia 26 JAN 2017

5 intermittent diarrhea 2

6 INCREASED OF TRANS

7 neutropenia 21 FEB 20

8 neutropenia 22 MAR 20

9 Platelet count decrease

10 fever 10 FEB 2017

11 intermittent diarrhea

12 fatigue 22 FEB 2017

13 anemia 22 MAR 2017

14 edema inferior limbs

15 deep vein thrombosis

16 neutropenia 31 MAY 2

17 intermittent platelet c

18 intermittent platelet c

19 anemia 09 MAY 2017

20

21 anemia 31 MAY 2017

22 intermittent platelet c

23 intermittent platelet c

24 intermittent anemia 1

25 intermittent platelet c

26 intermittent platelet c

27 leucopenia (lab findings) 23

28 neutropenia 23 AUG 2017

29 intermittent platelet c

30 intermittent platelet c

31 leucopenia 18 APR 201

32 anemia 18 APR 2017

33 leucopenia 21 JUL 20

34 neutropenia 21 JUL 20

35 Intermittent Anemia 1

36 Intermittent diarrhea

37 Leucopenia 18 JAN 20

38 leucopenia 20 SEP 20

ADVERSE EVENT

Adverse Event anemia

SAE? ☐ Yes ☒ No

Start Date (DD/MMM/YYYY) 31 MAY 2017

Outcome ☒ Ongoing ☐ Resolved (provide End Date) ☐ Death

If Resolved, was this due to change in seriousness/severity? ☒ Yes ☐ No

End Date (DD/MMM/YYYY) 15 JUN 2017

Toxicity/Severity Grade 2=Moderate

Relationship to Study Treatment - Ibrutinib/Placebo Unlikely Related

Relationship to Study Treatment - Nab-paclitaxel Possibly Related

Relationship to Study Treatment - Gemcitabine Possibly Related

Action Taken with Study Treatment ☐ Not applicable ☒ Dose not changed

SAE (serious adverse event)

COMPANY USE ONLY
Receipt date of this report
(stamp or date)

☐ Initial	☐ Follow-up
----------------------------------	------------------------------------

[REDACTED]

Reporter's First Name	Reporter's Last Name	
Investigator's First Name (if different from Reporter)	Investigator's Last Name (if different from Reporter)	
Address		City
Country	Phone Number	
E-Mail	Fax Number	

Subject ID		EMR 100070-003		/		/			
Trial No.		Center No.		Subject No.					
Subject Initials		Sex ☐ Female ☐ Male		Height cm		Weight kg			
Date of Birth (dd/mm/yyyy) OR Age at Time of Adverse Event (Specify unit, e.g. years/months, etc.)									
Ethnicity/Race ☐ American Indian/Alaska native ☐ Asian ☐ Black or African American ☐ Caucasian/White ☐ Hispanic or Latino ☐ Native Hawaiian or other Pacific Islander ☐ other _____									

Condition/Disorder	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Ongoing
	/ /	/ /	☐
	/ /	/ /	☐
	/ /	/ /	☐
	/ /	/ /	☐
	/ /	/ /	☐

Page 1 of 6

Study Information

- ### Subject Information

5. Medical history relevant to the SAE including concurrent and pre-existing conditions (please provide dates):

[illegible]

End of treatment (EOT)

```
graph TD; EOT[End of treatment (EOT)] --> ED[Early discontinuation]; EOT --> ECTC[End of treatment according to clinical trial]; ED --> T[Toxicity]; ED --> PD[PD]; ED --> CW[Consent withdrawal]; ED --> D[Death];
```

Early
discontinuation

End of treatment
according to clinical trial

Toxicity

PD

Consent
withdrawal

Death

THANK YOU FOR YOUR ATTENTION



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