IEO
Istituto Europeo di Oncologia

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

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

Studi clinici di imminente apertura

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

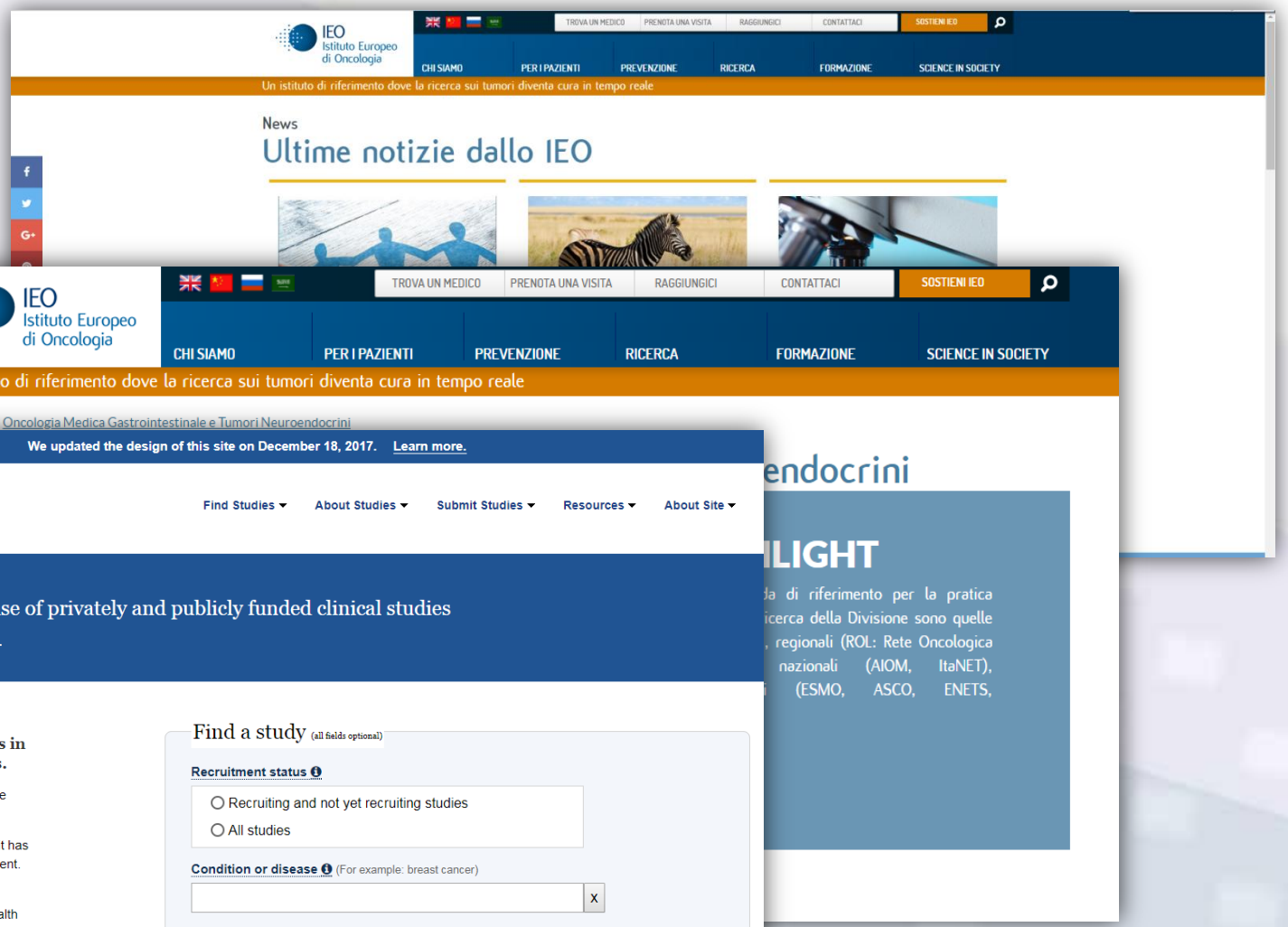
Studi clinici con arruolamento chiuso ma con pazienti in trattamento

Pancreas	**IEO 695** (phase IV) - sunitinib in advanced or metastatic PanNET **ROLLOVER** everolimus roll-over protocol **TALENT** (phase II) - Lenvatinib **PDR001** **IEO 694 - Radiant 4**
GEP NEN	**TALENT** **PDR001** **IEO 694 - Radiant 4**
Lung	**PDR001** **IEO 694 - Radiant 4** **LUNA** **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..



Team della Divisione di Oncologia Medica Gastrointestinale e Tumori Neuroendocrini

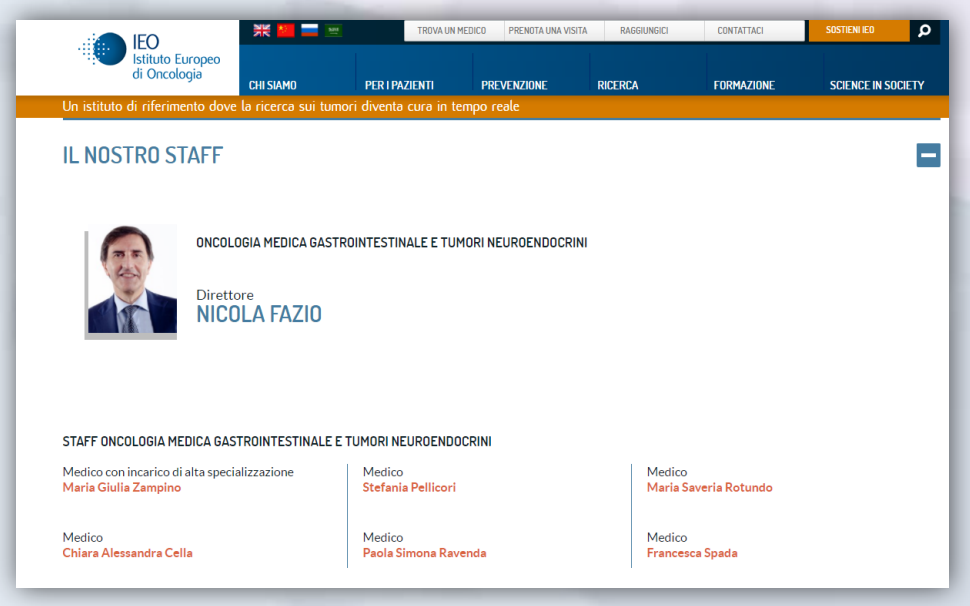
Direttore: Fazio Nicola

Medici ricercatori: Spada Francesca
Cella Chiara Alessandra
Rubino Manila
Pellicori Stefania
Laffi Alice
Pozzari Marta

Clinical Trial Coordinator : Tamayo Darina
Mazzon Cristina

Infermiera di ricerca: Gandini Antonella

Segretaria: Italia Paola



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

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- Programmazione e gestione delle procedure previste dalla sperimentazione
- Coordinamento di tutte le figure coinvolte all'interno del team IEO
- Raccolta ed analisi dei dati e della documentazione
- Elaborazione di data-base per la gestione dei clinical trials
- Mantenimento dei rapporti con gli Sponsor/CRO
- Assistenza inserimento dati
- Management farmaci e campioni biologici

Infermiera di ricerca

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- Assessment infermieristico (cartella elettronica)
- Gestione del farmaco sperimentale, educazione sanitaria (corretta conservazione ed assunzione del farmaco e stili di vita)
- Valutazione della compliance alla terapia (diario IEO)
- Raccolta dei campioni centralizzati (farmacocinetica e biomarkers)
- Somministrazione dei questionari di qualità di vita cartacei o tramite tablet
- Contatto telefonico con il paziente

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 cri

1. Signed written informed consent
2. Male or female subjects aged ≥ 18 y
3. Histologically proven MCC
   a. Confirmation of the diagnosis appropriate cytokeratin expres laboratory testing) in the tumo
   b. Subjects must have metastatic recurrent or unresectable are N entry
   c. For Part A: Subjects must hav of metastatic MCC and must h that was administered. Subj chemotherapy regimens for topotecan, doxorubicine, epir combination with carboplatin
   d. For Part B: Subjects must not MCC. Prior chemotherapy tr disease; no metastatic disease 6 months prior to study start

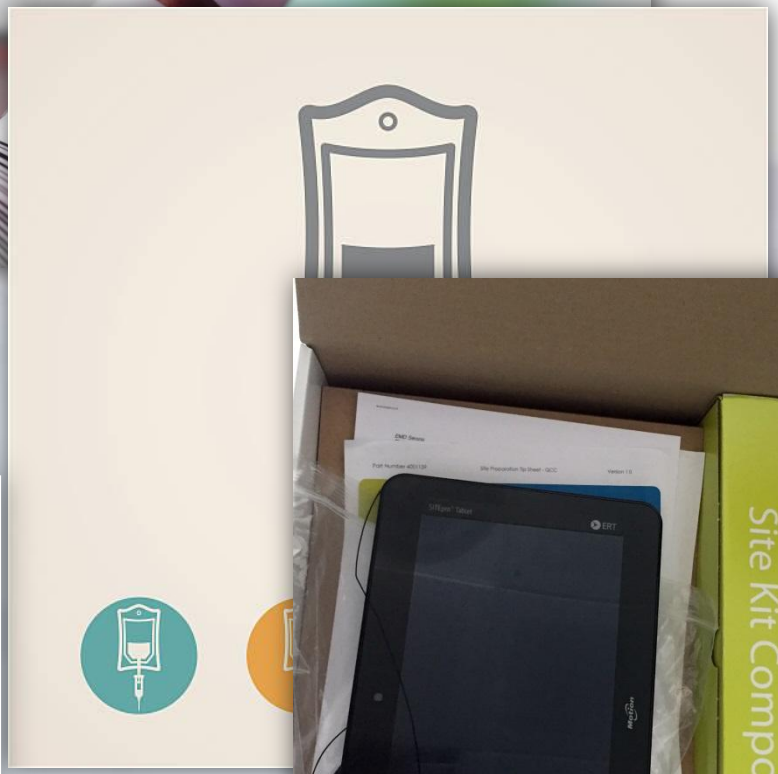
Exclusion Criteria

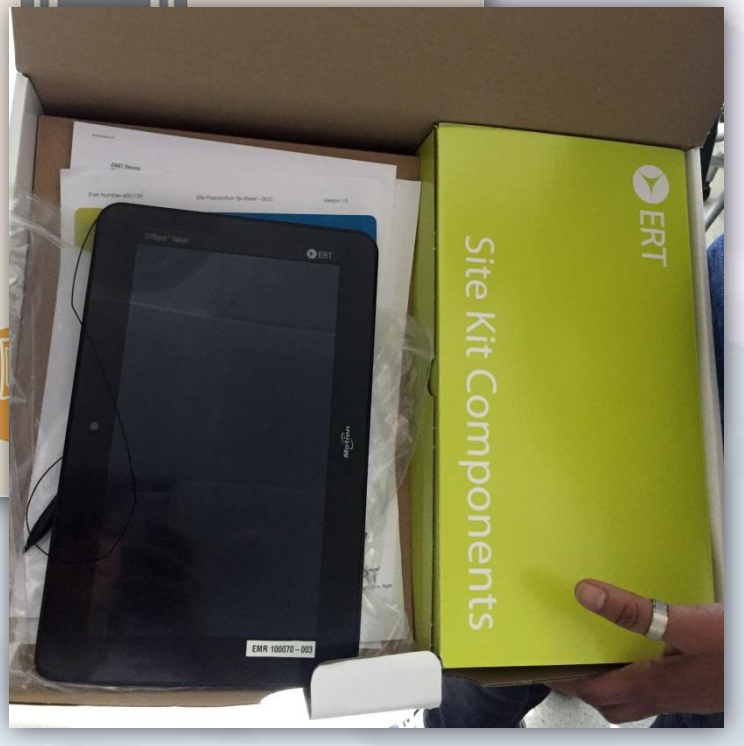
5.3.2

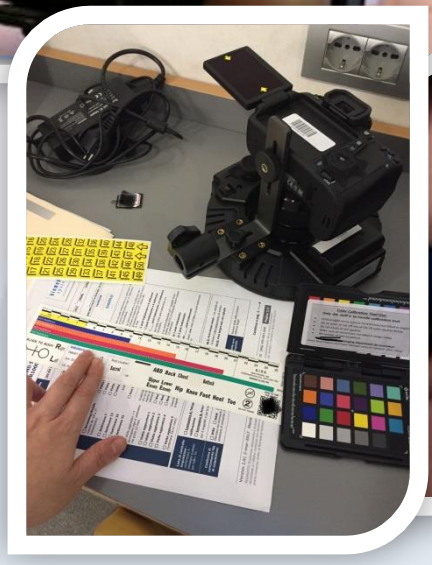
Subjects are not eligible for this trial if they fulfill any of the following exclusion criteria:

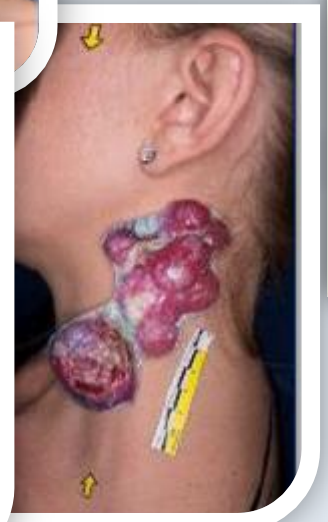
1. Participation in another interventional clinical trial within the past 30 days (participation in observational studies are permitted)
2. Concurrent treatment with a nonpermitted drug
3. Prior therapy with any antibody/drug targeting T-cell coregulatory proteins (immune checkpoints) such as anti-PD-1, 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 cen… …jects with a history of treated CNS m… …unless they have fully recovered fro… …months, and do not require continued

First day of treatment

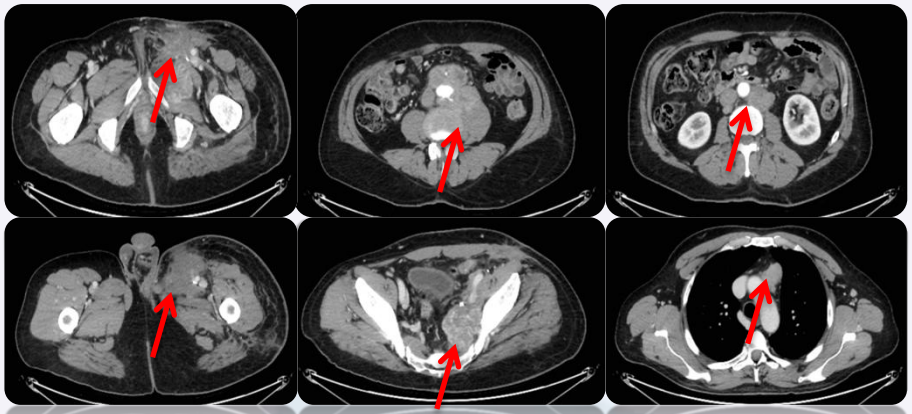


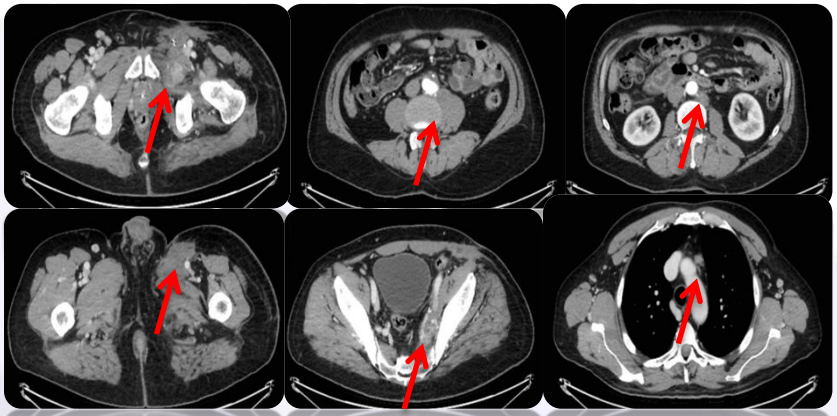




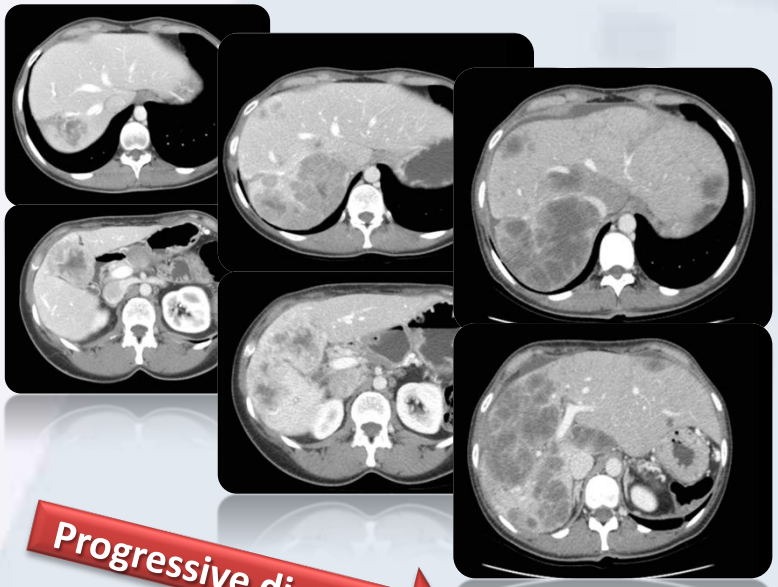


Assessment during the treatment





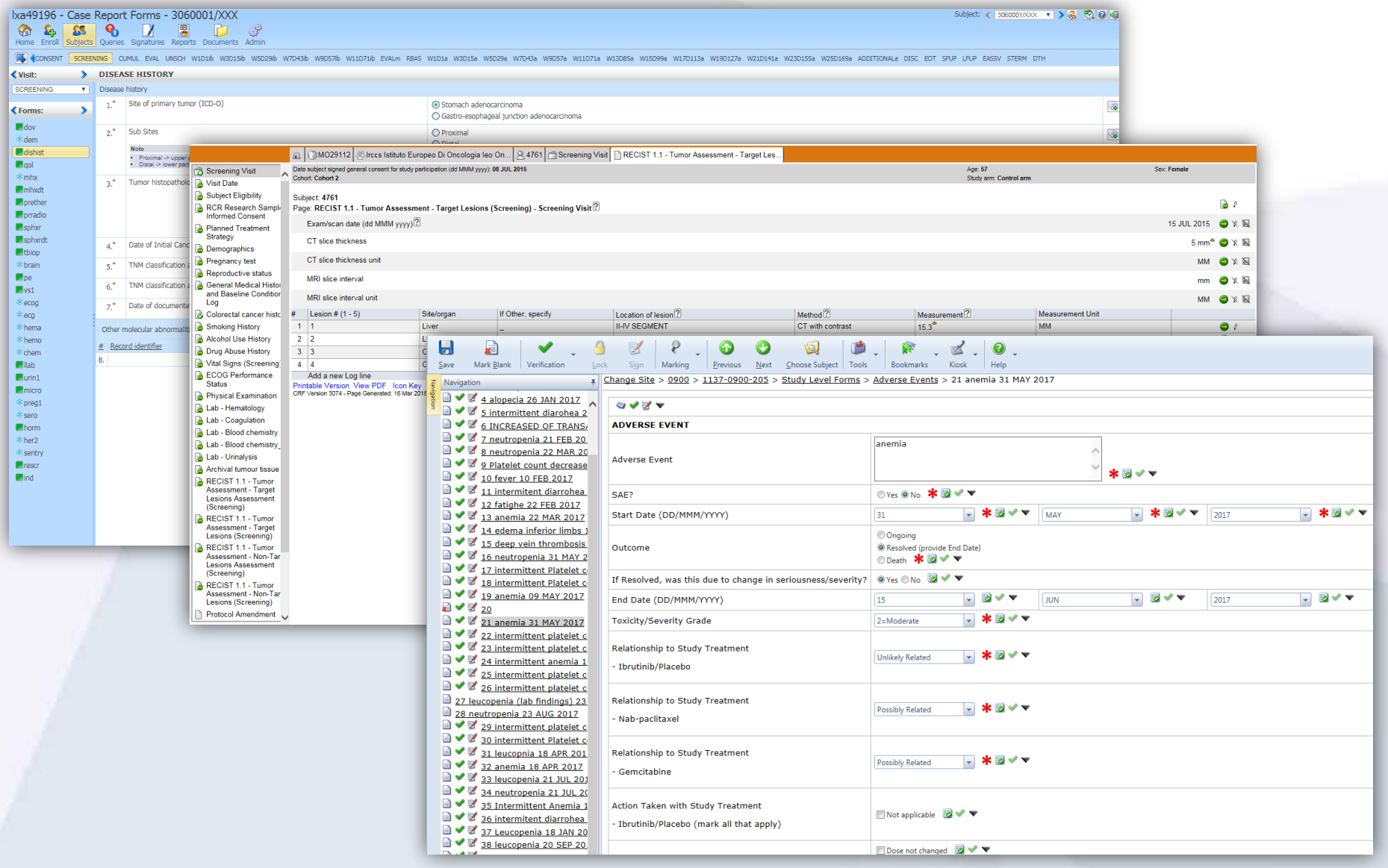
partial response



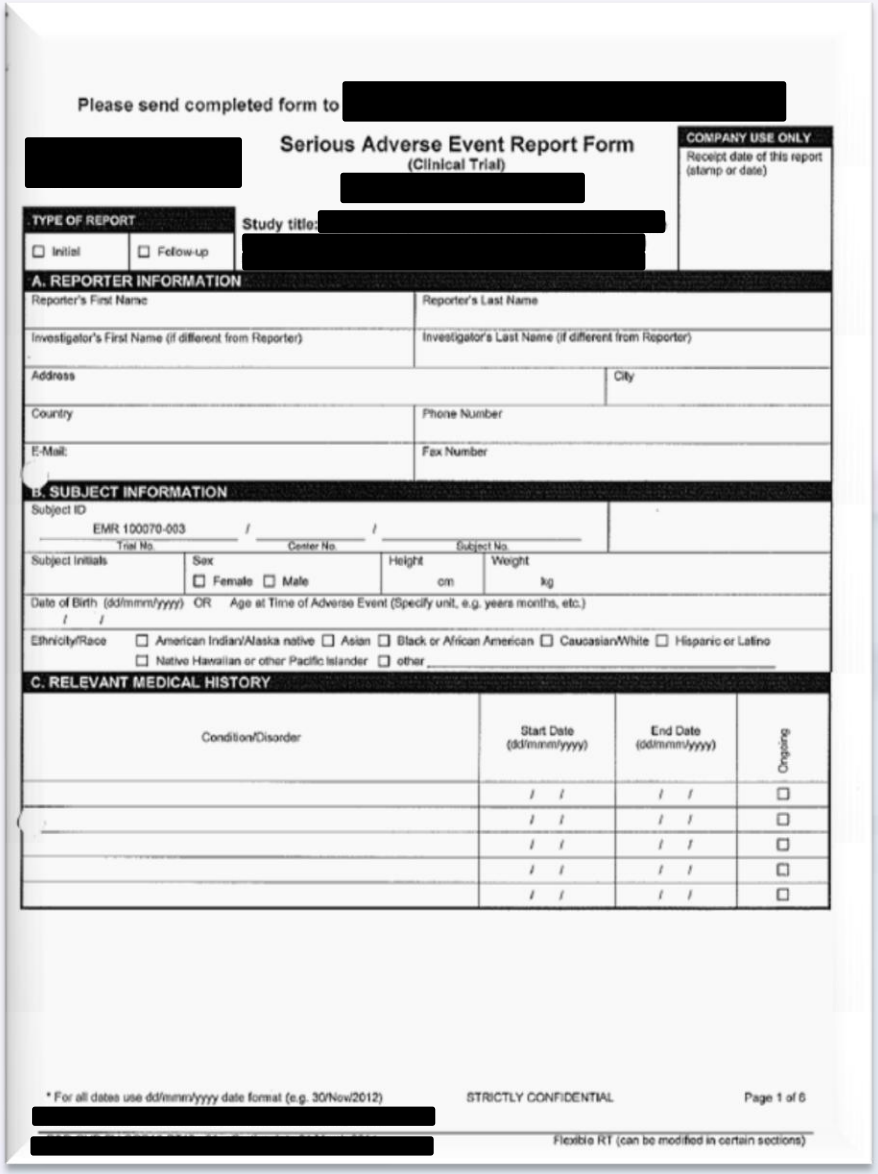
Progressive disease

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 ≥ 30% decrease from baseline TTB	**PR** ≥ 30% decrease from baseline TTB
SD = when neither PR nor PD can be established	**SD** = when neither PR nor PD can be established
PD ≥ 20% increase in the nadir of TTB (minimum 5 mm)	**PD** ≥ 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)



SAE (serious adverse event)



Please send completed form to [redacted]

[redacted]

Serious Adverse Event Report Form
(Clinical Trial)

[redacted]

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

TYPE OF REPORT: ☐ Initial ☐ Follow-up

Study title: [redacted]

A. REPORTER INFORMATION

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

B. SUBJECT INFORMATION

Subject ID: EMR 100070-003 / ____ / ____ (Trial No. / Center No. / Subject No.)

Subject Initials	Sex	Height	Weight
	☐ Female ☐ Male	cm	kg

Date of Birth (dd/mmm/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 ____

C. RELEVANT MEDICAL HISTORY

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

* For all dates use dd/mmm/yyyy date format (e.g. 30/Nov/2012)

STRICTLY CONFIDENTIAL

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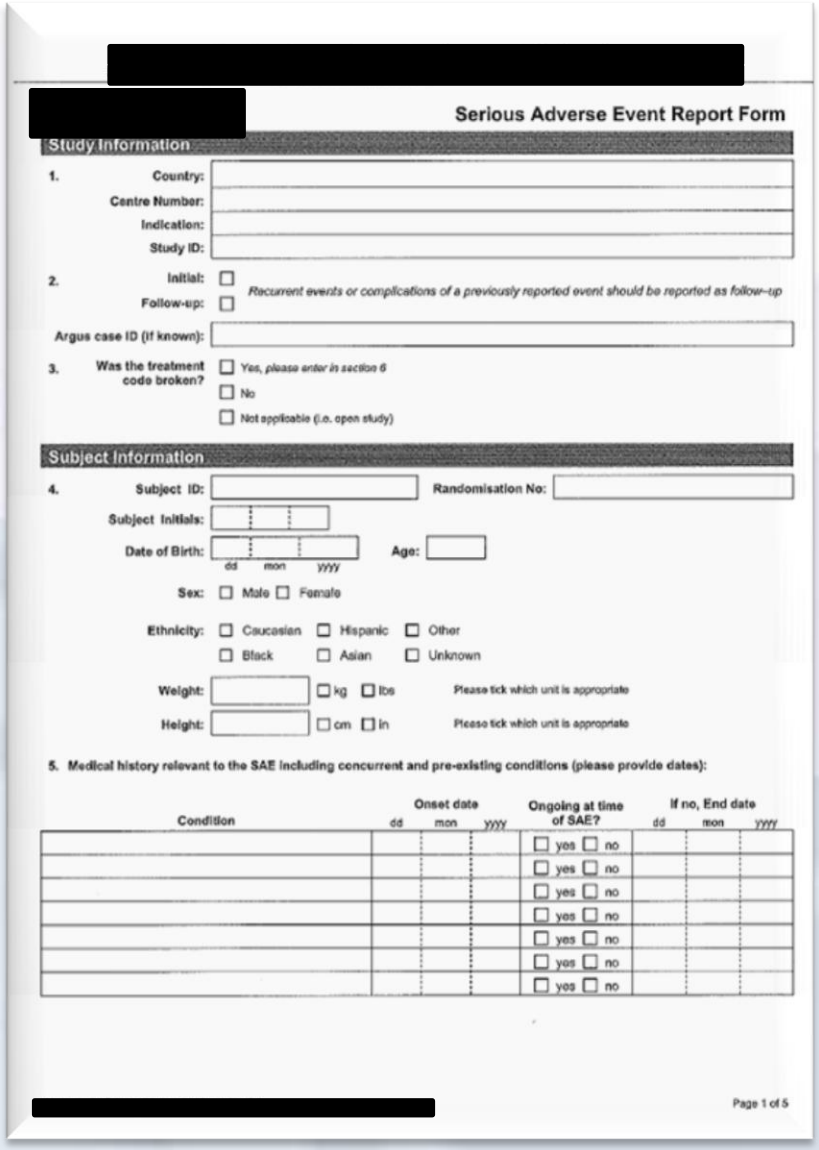
Flexible RT (can be modified in certain sections)



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Serious Adverse Event Report Form

Study Information

1. Country: ____
   Centre Number: ____
   Indication: ____
   Study ID: ____

2. Initial: ☐
   Follow-up: ☐
   Recurrent events or complications of a previously reported event should be reported as follow-up

Argus case ID (if known): ____

3. Was the treatment code broken? ☐ Yes, *please enter in section 6* ☐ No ☐ Not applicable (i.e. open study)

Subject Information

4. Subject ID: ____ Randomisation No: ____

Subject Initials: ____

Date of Birth: ____ (dd mon yyyy) Age: ____

Sex: ☐ Male ☐ Female

Ethnicity: ☐ Caucasian ☐ Hispanic ☐ Other ☐ Black ☐ Asian ☐ Unknown

Weight: ____ ☐ kg ☐ lbs Please tick which unit is appropriate

Height: ____ ☐ cm ☐ in Please tick which unit is appropriate

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

Condition	Onset date dd	mon	yyyy	Ongoing at time of SAE?	If no, End date dd	mon	yyyy
				☐ yes ☐ no			
				☐ yes ☐ no			
				☐ yes ☐ no			
				☐ yes ☐ no			
				☐ yes ☐ no			
				☐ yes ☐ no			
				☐ yes ☐ no			

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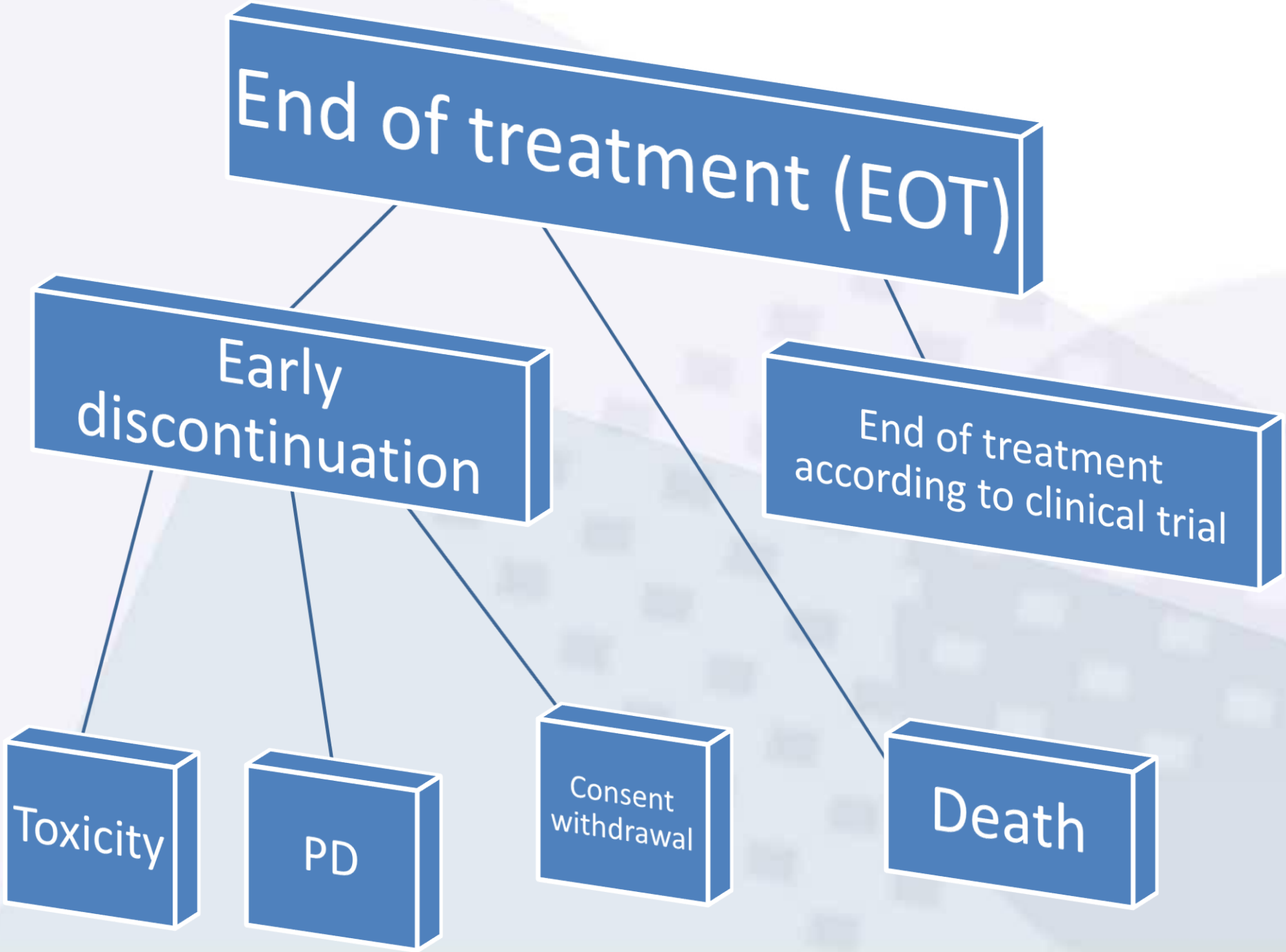
End of treatment (EOT)
Early discontinuation
End of treatment according to clinical trial
Toxicity
PD
Consent withdrawal
Death

THANK YOU FOR YOUR ATTENTION

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