MaNGO

XVII ASSEMBLEA MaNGO

MILANO

16 OTTOBRE 2020

Con il Patrocinio di:

SIGO SOCIETA' ITALIANA DI GINECOLOGIA E OSTETRICIA

SIOG SOCIETÀ ITALIANA DI ONCOLOGIA GINECOLOGICA

FICOG Federation of Italian Cooperative Oncology Groups

ACTO

Studio AtTEnd

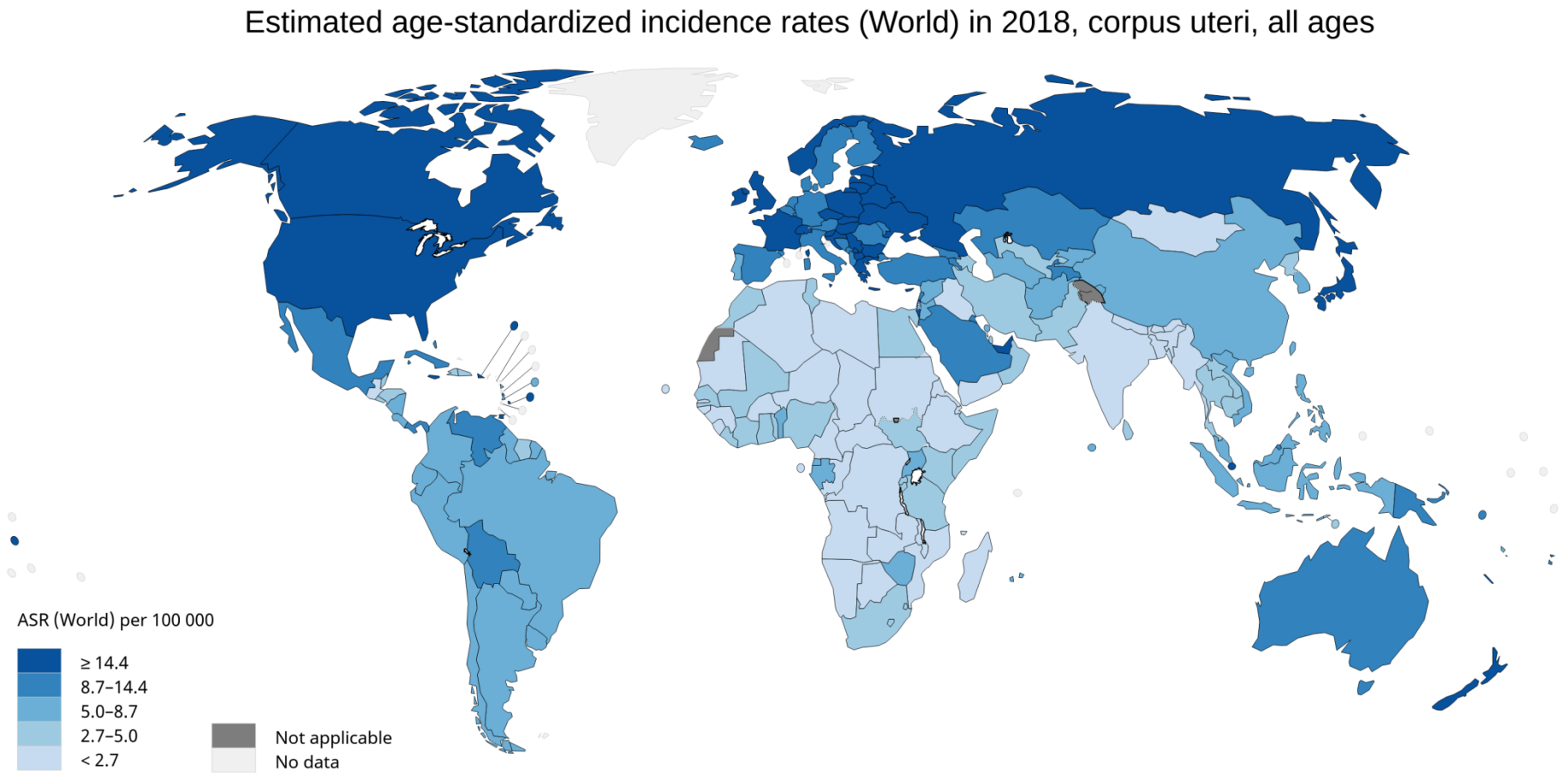
Phase III double-blind randomized trial of atezolizumab in combination with paclitaxel and carboplatin in women with advanced/recurrent endometrial cancer

Stato di avanzamento

Dott.ssa Maria Elena Laudani
Prof. Paolo Zola
Dipartimento di Scienze Chirurgiche
Università degli Studi di Torino

ENDOMETRIAL CANCER

Epidemiology



Data source: GLOBOCAN 2018
Graph production: IARC (http://gco.iarc.fr/today)
World Health Organization

In 2018

- 382 069 new cases of endometrial cancer diagnosed
- 89.929 endometrial cancer-related deaths globally

RATIONALE FOR STUDY DESIGN

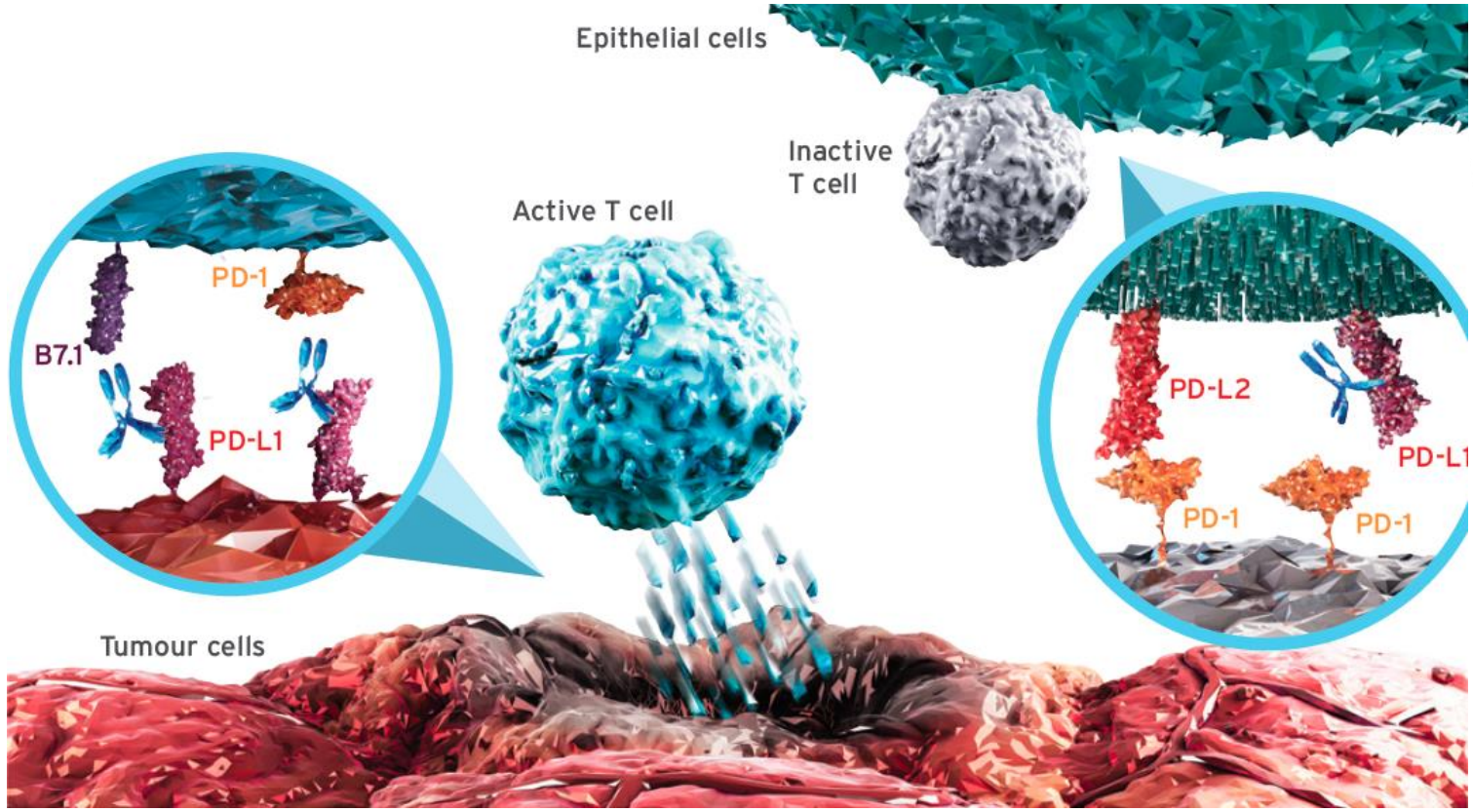
Advanced and/or recurrent endometrial cancer has a poor prognosis: paclitaxel + carboplatin is the standard of care (median PFS: 8-12 months)

Rationale for immunotherapy

- Endometrial cancers have high mutational load
- *POLE*-mutated and MSI tumors exhibited significantly elevated TILs, higher expression of PD-1 and PD-L1; greater peritumoralT-lymphocytes compared to MSS tumors.
- Mismatch-repair deficiency has increased number of mutation-associated neoantigens
- Mismatch-repair deficiency is present in 20-30% endometrial cancers
- POLE mutations occur in approximately 6% of endometrial cancers

ATEZOLIZUMAB

PD-L1 is expressed on tumour cells and tumour infiltrating immune cells.
Binding of PD-L1 to its receptors PD-1 and B7.1 can lead to the inhibition of anticancer T-cell activity in the tumour



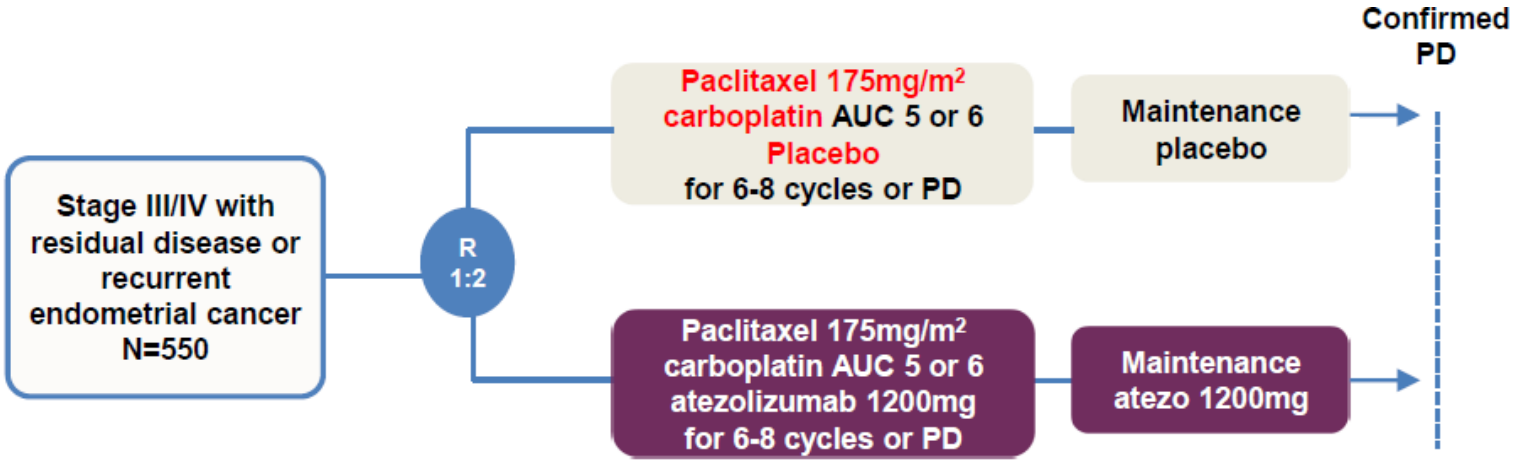
https://www.roche4med.co.il/products/tecentriq/mechanism-of-action.html

Atezolizumab is an engineered humanised monoclonal immunoglobulin G1 antibody that binds selectively to PD-L1 and prevents its interaction with PD-1 and B7-1 (CD80).

STUDY DESIGN

Primary objective: OS and PFS

Secondary objectives: PFS in MSI, PFS2, RR, QoL, safety



Stratified by:

- Country of the experimental center
- Histological type (endometrioid vs. other types)
- Disease (recurrent disease vs advanced disease at primary diagnosis)
- MS status (MSS vs MSI vs non-evaluable)

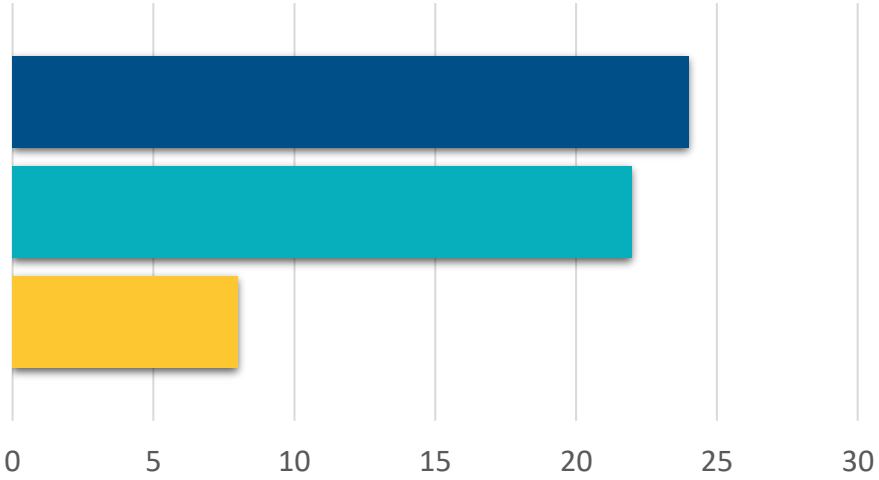
OUR EXPERIENCE

CITTA' DELLA SALUTE E DELLA SCIENZA DI TORINO – P.O. SANT'ANNA

Principal Investigator: Paolo Zola

AZIENDA OSPEDALIERO - UNIVERSITARIA
Città della Salute e della Scienza di Torino

Enrollment status

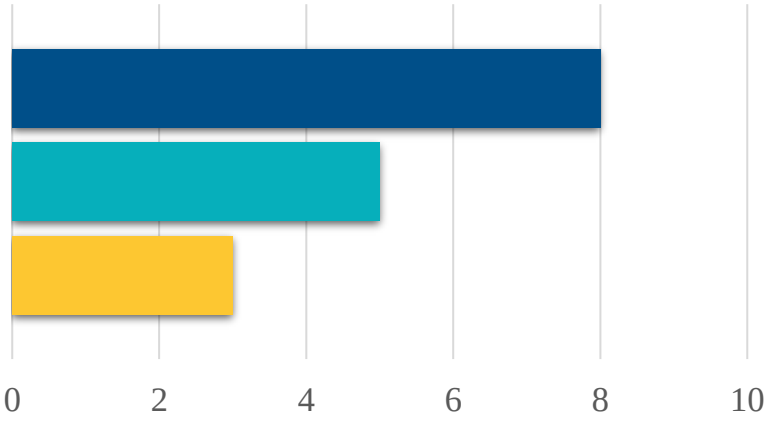


	enrollement status
Screened	24
Enrolled	22
Discontinued	8

- 14 patients are under treatment
- 7 patients are in the maintenance phase
- 5 patients discontinuated for progression
- 3 patients discontinuated for Serious Adverse Event

- First patient enrolled on 1st March 2019
- Enrollments have been continued also during Covid period without substantial changes
- 23 patients have been screened
- 2 patients are under screening

Discontinuation



	Discontinuation
Discontinued	8
Disease Progression	5
SAE	3

ADVERSE EVENTS MANAGEMENT

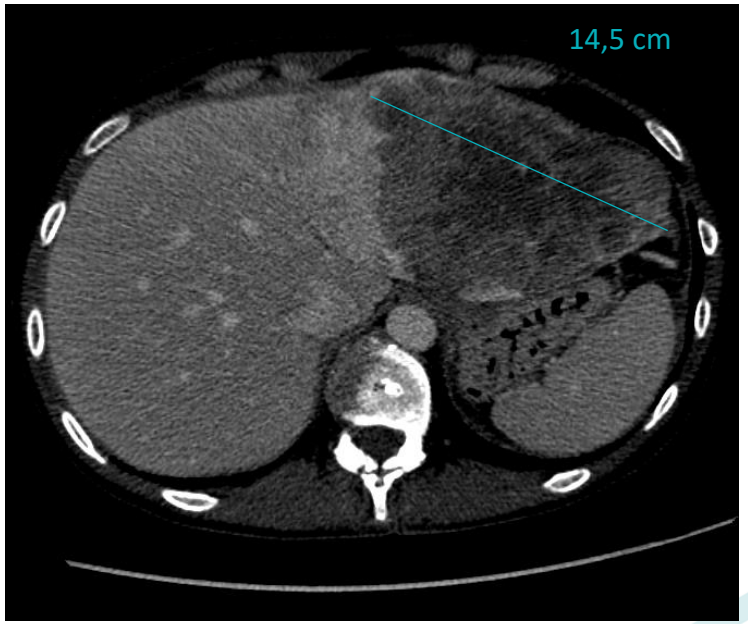
- Most frequent AE are NCI CTCAE grade 1 or 2
- Most common AE are haematological (anemia, neutropenia, thrombocytopenia) as per standard chemotherapy
- Supportive care such as therapy delay, iron supply, EPO, blood trasfusion, G-CSF is usually sufficient
- SAE usually need specific therapy and/or hospitalization (e.g. acute renal failure requiring steroid therapy and/or dialysis)

STRENGTHS

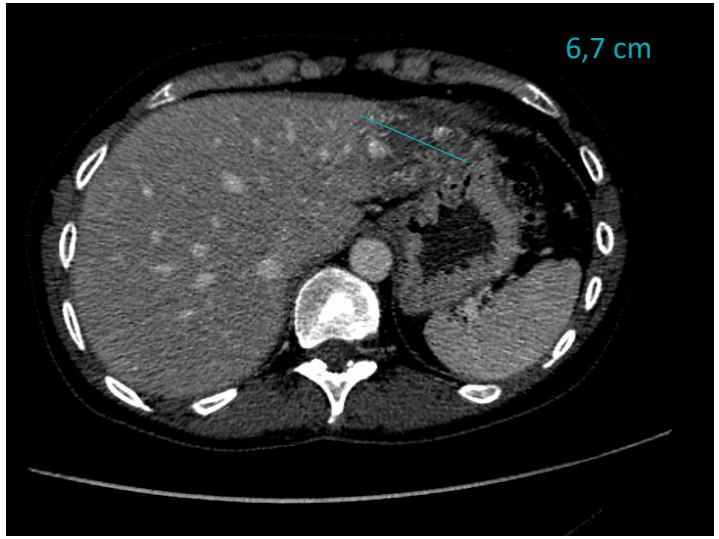
- Excellent communication with the Sponsor
- Constant collaboration with Central staff and Study Monitors
- Adaptation of treatment schedule to patients' needs
- Excellent collaboration with all the involved figures (study coordinators, nurses, pharmacists, radiologists and other professional figures)

CLINICAL CASE

- A.C., 40 years, ECOG 0, no relevant medical history, nulliparous
- Stage at diagnosis: IV B, Endometrioid
  - Target lesions in the pelvis
  - Liver metastasis of 145 mm
  - No non-target lesions



- At cycle 2 paclitaxel related AE → substituted with docetaxel at cycle 3
- At cycle 3 carboplatin related AE → substituted with cisplatin at cycle 4
- Patient received 8 cycles of standard chemotherapy + Atezolizumab/placebo and 2 cycles of maintenance
- At disease assessment: PR in accord to RECIST



- Surgery performed after Sponsor Approval → R0 after surgery
- Histological response: no evidence of disease (ypT0N0M0)
- Maintenance phase restarted at 4-5 weeks from surgery

Studio AtTEnd

Phase III double-blind randomized trial of atezolizumab in combination with paclitaxel and carboplatin in women with advanced/recurrent endometrial cancer

Study update

XVII Assemblea MaNGO – Milano 16 ottobre 2020

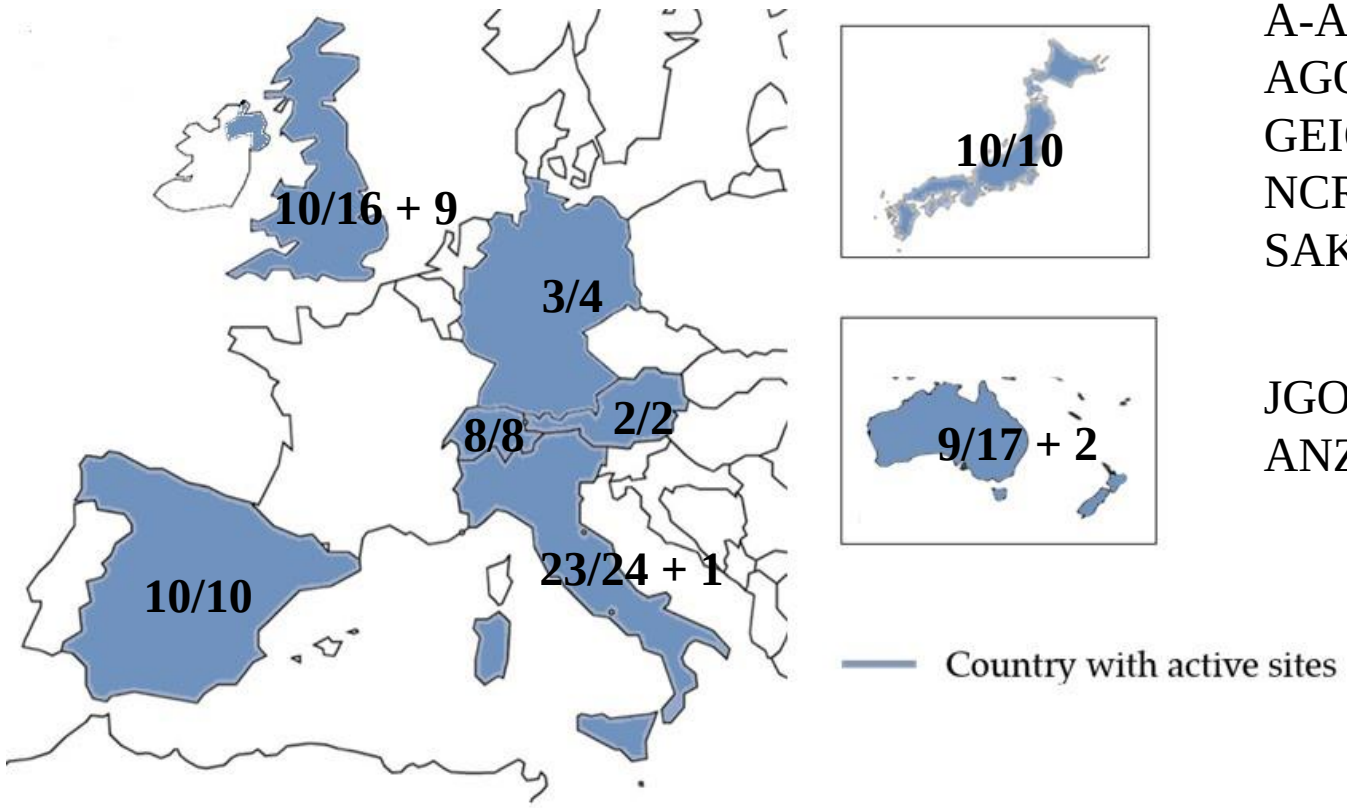
Anna Roberto

Laboratorio di Metodologia per la ricerca clinica

Istituto di Ricerche Farmacologiche Mario Negri IRCCS

OVERVIEW ON GLOBAL STUDY ACTIVATION

Sites, overall: 75 open sites/91 involved (82%)



Participating Groups:

MaNGO – Italy
A-AGO – Austria
AGO – Germany
GEICO – Spain
NCRI – UK
SAKK – Switzerland

JGOG – Japan
ANZGOG – Australia New Zealand

OVERVIEW ON GLOBAL ENROLLMENT STATUS

ACTIONS TO INCREASE ENROLLMENT RATE

- Patient fee increase
- Involvement of the ThreeWire company
- Communication plan reinforced
- Increase committment (Japan and Spain)

+ New collaborations

KGOG - South Korea and TGOG – Taiwan

+ Possible new collaborations

GINECO – France and UGOS – Serbia

WHAT TO DO: about 27 pts/month

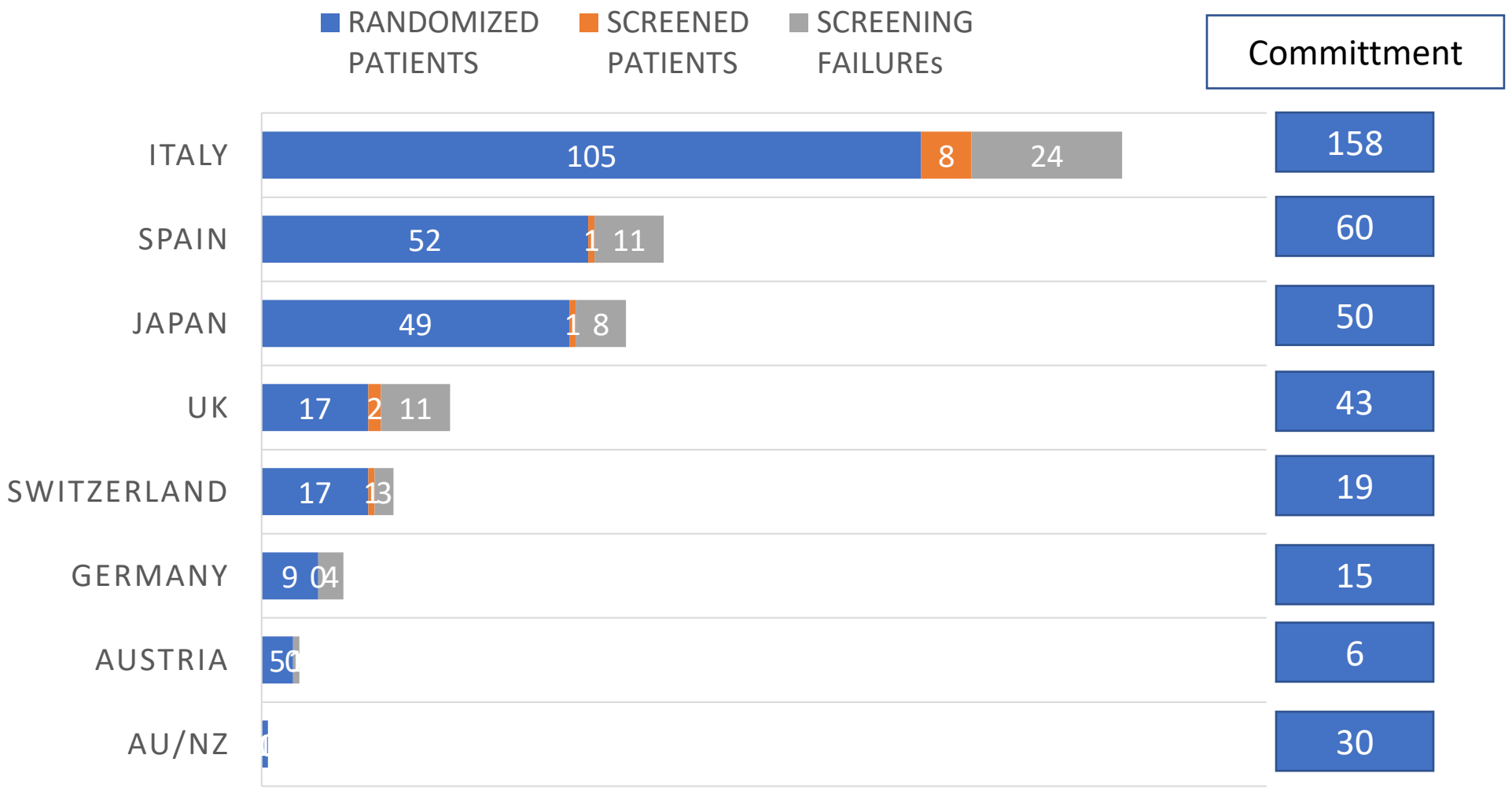
lment extension up to
021

n sent out on 14 September

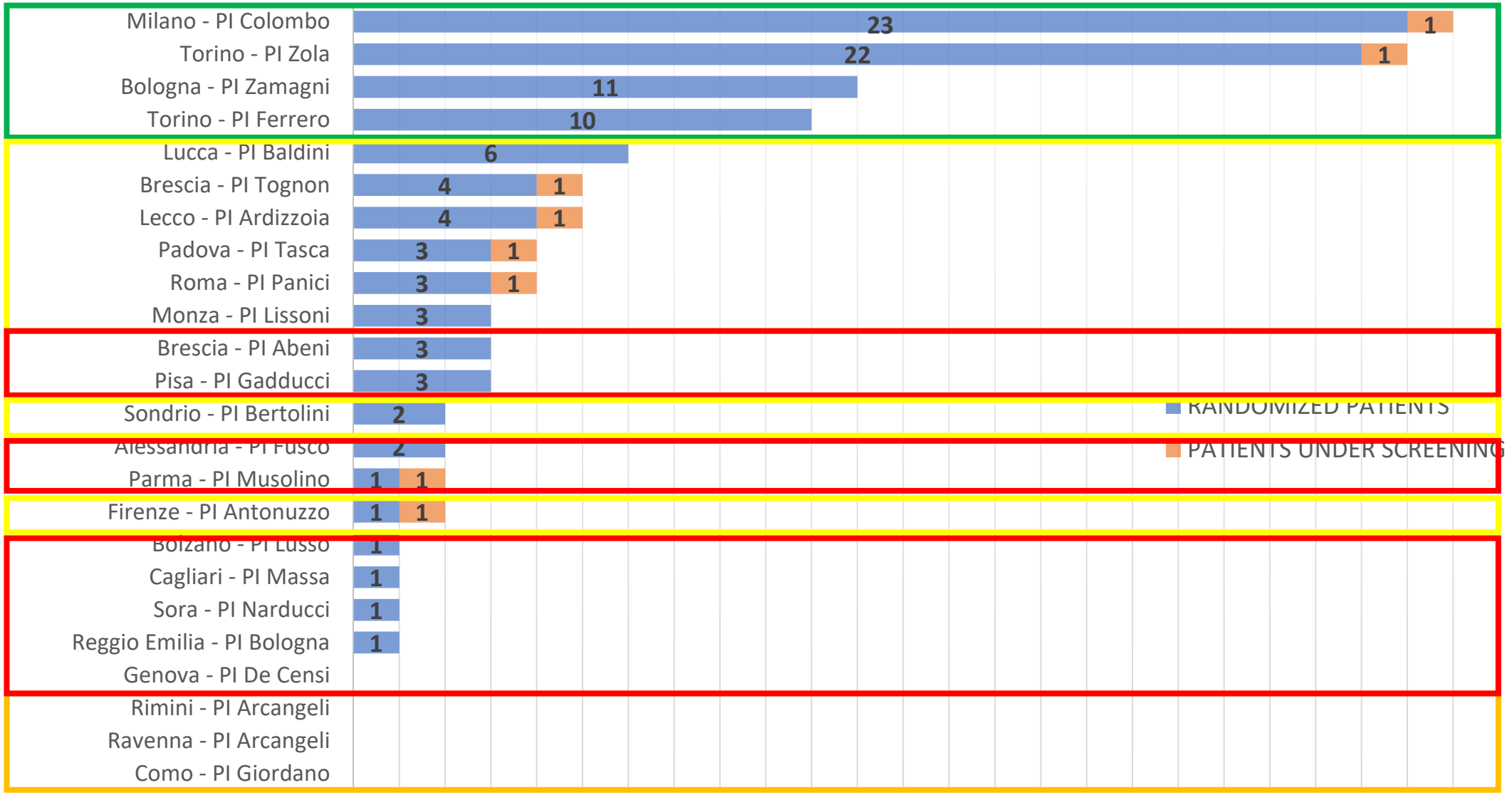
r 15th 2020:

domized patients: 255
eening failures: 62 (19%)
under screening: 13

ENROLLMENT BY COUNTRY AND COMMITMENT



ENROLLMENT BY ITALY



COVID-19 EMERGENCY

Measures in place to manage the emergency

- Exceptional measures for the management of the study have been released in accordance to EMA and ENGOT guidelines (regarded as urgent amendment in Italy and Germany)
- The recruitment of the trial remained open
- Prospectively anticipated protocol violations were not allowed, expecting all included patients to meet trial eligibility criteria
- A certain flexibility in the performance of lab tests/physical examinations in local structures was allowed for visits subsequent to the screening and baseline ones

Impact on enrollment

- 4 sites have officially suspended the recruitment
- A decrease in enrollment rate was observed for all other recruiting sites
- Opening of new sites in UK was blocked
- In AU/NZ all activations were further delayed

- 1 patient has been reported as COVID-19 positive

AMENDMENT STATUS UPDATE

Ongoing - Protocol v 4.0

Blood samples collection to evaluate the atezolizumab Pharmacokinetics, to determin the Anti-Therapeutic Antibody levels, and to identify the ct-DNA (as predictive/prognostic biomarker)

Group	Status	Approval date
AGO	Approved	13/08/2020
AGO-A	Approved	15/05/2020
GEICO	Approved	13/07/2020
NCRI - UK	Approved	02/07/2020
JGOJ	Approved	Jul-Aug/2020
ANZGOG	Approved REC	13/08/2020
MaNGO	Submitted	Dec 2020
SAKK	Submitted	


Thank you!