
XXXIII CONGRESSO NAZIONALE AIRO
AIRO2023
BOLOGNA,
27-29 OTTOBRE 2023
PALAZZO DEI CONGRESSI
Radioterapia Oncologica: l'evoluzione al servizio dei pazienti
Associazione Italiana
Radioterapia e Oncologia clinica

XXXIII CONGRESSO NAZIONALE AIRO

AIRO2023

BOLOGNA,
27-29 OTTOBRE 2023
PALAZZO DEI CONGRESSI

Radioterapia Oncologica: l'evoluzione al servizio dei pazienti

PREOPERATIVE SINGLE-FRACTION RT FOR EARLY-STAGE BC: PRELIMINARY RESULTS FROM CRYSTAL PHASE I/II STUDY

AIRC 2019 IG Id.23118

Dott.ssa Maria Alessia Zerella

G.C.Mazzola, M.Zaffaroni, G.Ronci, S.Dicuonzo, D.P.Rojas, A.Morra, M,A. Gerardi, C.Fodor, E.Rondi, S.Vigorito, S.Penco, M.Sargenti, P.Baratella, E.Vicini, C.Morigi, S.Kahler-Ribeiro-Fontana, V.E. Galimberti, S.Gandini, E.De Camilli, G.Renne, F.Cattani, P.Veronesi, R.Orecchia, B.A.Jereczek-Fossa, M.C.Leonardi

European Institute of Oncology - IRCCS - Milan

Associazione Italiana
Radioterapia e Oncologia clinica

DICHIARAZIONE

Relatore: Dott.ssa Maria Alessia Zerella

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Consulenza ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazione ad Advisory Board **(NIENTE DA DICHIARARE)**
- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Altro

Background

Breast-conserving surgery (BCS) and WBRT are the standard of care for early-stage BC

Accelerated Partial Breast Irradiation has been gaining ground as an attractive alternative in selected patients with low-risk BC

Clinical t**RI**Al on **S**ingle fraction ablative preoperative radiation **T**reatment for e**A**r**L**y-stage breast cancer (CRISTAL)

- preoperative RT
- single fraction
- CyberKnife
- selected patients

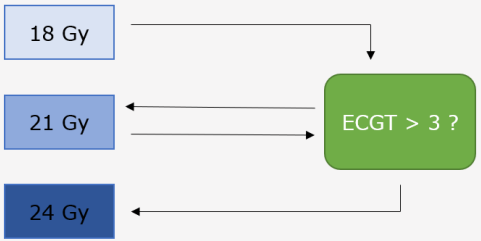
AIRC
Rendiamo il cancro sempre più curabile.

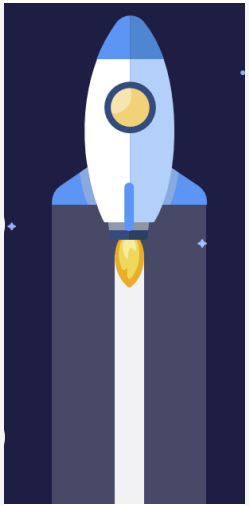
IEO
Istituto Europeo di Oncologia

Study Design: Phase I-II study

Phase I: dose escalation
(2 years)

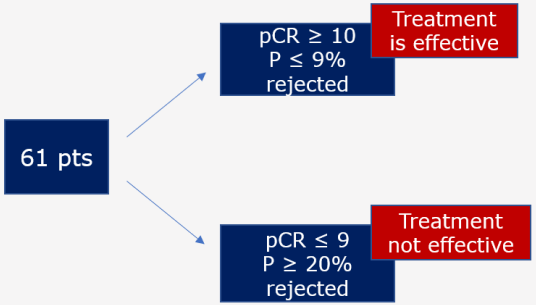
- dose-escalation 18/21/24 Gy
- isodose between 80% and 90%
- Cohort: max 18 pts
- **AIM:** identification of the **maximum tolerated dose** (**MTD**) ,CTCAE skin toxicity grade <3





Phase II: pCR
(3 years)

- The MTD identified in the first phase is administered
- Cohort: 61pts
- **AIM:** Evaluation of the effectiveness of preoperative treatment for ablative purpose, by the means of **pathological complete response rate** (no tumor in the surgical specimen)



Overview of the study protocol

Zerella et al. BMC Cancer (2022) 22:358
https://doi.org/10.1186/s12885-022-09305-w

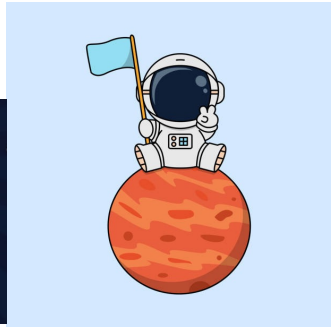
BMC Cancer

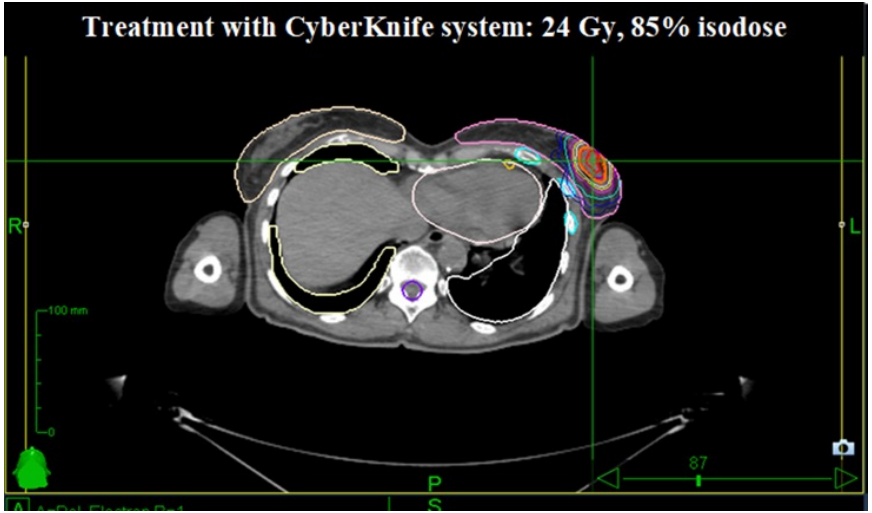
STUDY PROTOCOL Open Access

Single fraction ablative preoperative radiation treatment for early-stage breast cancer: the CRYSTAL study – a phase I/II clinical trial protocol

Maria Alessia Zerella[1], Mattia Za… Dicuonzo[1], Damaris Patricia Rojas[1], Anna Morra[1], Cristiana Fodor[1], E… sca Botta[2], Marta Cremonesi[3], Cristina Garibaldi[3], Silvia Penco[4] …ra[5], Sara Gandini[6], Massimo Barberis[7], Giuseppe Renne[7], Federica Catt… …hia[9], Barbara Alicja Jereczek-Fossa[1,8] and Maria Cristina Leonardi[1*]

n
BI





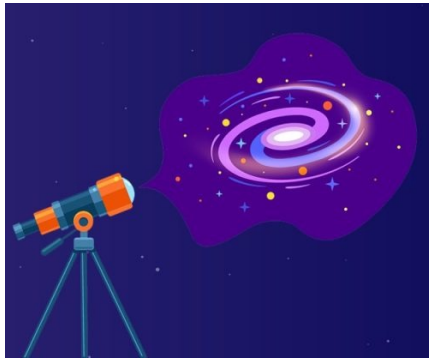
9 patients treated with Cyberknife system

- 3 patients recieved 18 Gy, 85% isodose
- 3 patients received 21 Gy, 85% isodose
- 3 patients received 24 Gy, 85% isodose

maximum tolerated dose identified →

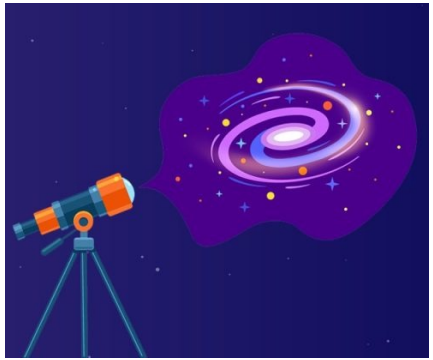
24Gy

Phase II is open, with 5 patients treated



RESULTS 1

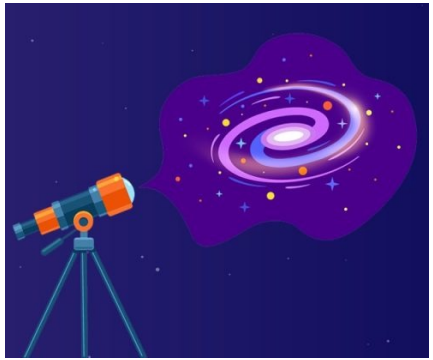
- 9 patients were treated within the phase I of the study (3 patients for each dose step: 18-21-24 Gy) while 5 were treated within the phase II with 24 Gy in single fraction
- Median age at enrollment was 66.8 years (IQR 63.4 – 69.0)
- Stage at diagnosis was cT1N0 for 8 patients and cT2N0 for 6 patients
  - Invasive ductal carcinoma for 13 patients and 1 lobular carcinoma
  - luminal A for 10 patients
  - luminal B for 1 patient
  - luminal B-HER2+ for 2 patient
  - triple negative for 1 patient
- Comparing pre-RT MRI and pre-surgery MRI according RECIST criteria
  - 7 patients experienced stability disease
  - 4 patients experienced a partial response
  - 1 patient experienced a complete response



RESULTS 2

- Median time to surgery was 33 days (range 28 – 40 days)
  - 3 patients underwent mastectomy+snlb
  - 11 patients underwent quadrantectomy+snlb
- A post-surgical complication has been reported in 1 patient (liponecrosis)
- All patients except one experienced a reduction in Ki67 proliferation index (median change between biopsy and histologic exam of 7%)
- No pathological complete responses were observed
- Response evaluation according RECIST criteria (tumor size on pre-RT MRI vs definitive histology)
  - no complete response and no progression disease
  - 7 patients experienced stability disease
  - 7 patients experienced a partial response with a downstaging from stage IIA to IA

MEDIAN RESIDUAL TUMOUR CELLULARITY was 40% (data available for 5 patients)



RESULTS 3

- 11 patients have received post-operative RT and 2 of them have received also chemotherapy
- At last follow-up has been reported only one G1 chronic toxicity (breast pain) and no G>2 acute toxicities
- At a medium follow up of 13.1 months (range 1.4 – 23.3 months):
  - 1 patient developed a regional relapse (pN0 at surgery)
  - 2 patients developed a second tumor in another site
  - all the other patients are alive with no evidence of disease

- **MRI-histology correlation studies «historadiomics»**
- **Pathology and molecular pathology Task**

Pathology and molecular pathology Task

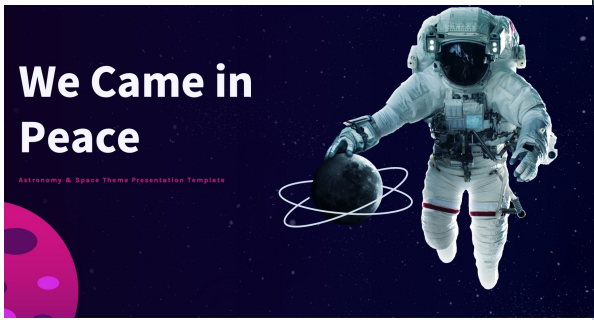
CORE BIOPSY ASSESSMENT, BEFORE RADIOABLATION TREATMENT			
Radiological sampling of the neoplasm	At least 5 cores (14 Gauge)	2+2 cores on 2 bio cassettes FF 1 core (ON FISOLOGIC	ROUTINE: NO
immediate biobank and gross pathology samples transfer			ROUTINE: NO
Histology assessment At least 4 cores (14 Gauge) on 2 bio cassettes FF	histology, grade H.E. Routine biological parameters	hormonal receptor, Her2/neu , Ki-67 index	ROUTINE: YES
	Extra parameters	tumor infiltrating lymphocytes (TILs) + PDL1	ROUTINE: NO
Molecular assessment At least 1 core NO-FF	frozen at IEO biobank	Qualitative and quantitative assessment of tumor DNA/RNA at baseline	ROUTINE: NO

POST-SURGICAL ASSESSMENT, 4-8 WEEKS AFTER RADIOABLATION TREATMENT			
post radiation Molecular assessment At least 3 core NO-FF	frozen at IEO biobank	baseline Qualitative and quantitative assessment of tumor DNA/RNA at	ROUTINE: NO
RMI Postoperative assessment	RMN sul pezzo operatorio. (ev. togliere clips metalliche)	Fissato in contenitore con Agar/Gel-ECO 3T x 30 min Risoluzione <0,5 mm	ROUTINE: NO
Grossing assessment	2 day After of formalin fixed sagittal cuts on orientable samples	include whole bio cassettes (IN TOTO)	ROUTINE: NO
Histology assessment	histology, grade H.E. Extent of residual disease in the posttreatment surgical resection	Modified# Residual Cancer Burden (RCB) index *(#WITHOUT LYMPH STATUS)*	Routine: YES
Histology assessment	tumor infiltrating lymphocytes (TILs), P	H.E. [25]	ROUTINE: NO
IHC analysis	Routine biological parameters Biological parameters	hormonal receptor, Her2/neu, Ki-67 index	Routine: YES
Others IHC analysis to assess neoplastic cellularity after therapy	To evaluate pathways of Apoptosis To evaluate hypoxia Response To evaluate specific Lymphocyticresponse	Anti-Caspase activate 3* HIF-1-alfa Routine: CD8 and/or CD4, CD20 (only responders: 1/3 of cases expected) PD1: PD-L1 expression	ROUTINE: NO
gene expression profiling in post radiation surgical samples	Oncomine Immune Response Research Assay	Table 3 List of 395 genes	ROUTINE: NO

Function	Number of genes
Antigen presentation	3
Antigen processing	19
Innate immune response	11
Leukocyte inhibition	2
Leukocyte migration	5
Lymphocyte activation	2
Lymphocyte development	3
Lymphocyte infiltration	46
B cell receptor signaling	3
T cell receptor signaling	6
T cell regulation	9
TCR coexpression	19
Chemokine signaling	10
Cytokine signaling	15
Interferon signaling	8
Type I interferon signaling	8
Type II interferon signaling	23
Housekeeping	11

Function	Number of genes
B cell marker	11
Dendritic cell	7
Dendritic cell, macrophage	6
Helper T cells	8
Macrophage	5
Myeloid marker	7
Neutrophil	5
NK cell activation	8
NK cell marker	4
T cell differentiation	2
Checkpoint pathway	30
PD-1 signaling	9
Drug target	21
Adhesion, migration	14
Apoptosis	4
Proliferation	10
Tumor antigen	17
Tumor marker	27

- **MRI-histology correlation studies «historadiomics»**
- **Pathology and molecular pathology Task**



Surgeons

Radiation oncologists

NO post-operative RT in luminal A

Conclusions

The present analysis reports preliminary results of the Crystal trial; data about late toxicities will be collected when updated follow-up data will become available

Phase II is in progress

This findings, updated with additional patients and longer follow-up, along with the data that will become available from similar ongoing investigations, may serve as a hypothesis-generating step towards a change of the current treatment paradigm in early stage BC

AIRC
Rendiamo il cancro sempre più curabile.

IEO
Istituto Europeo di Oncologia

AIRO2023

Radioterapia Oncologica:
l'evoluzione al servizio dei pazienti


XXXIII CONGRESSO NAZIONALE AIRO
AIRO2023
BOLOGNA,
27-29 OTTOBRE 2023
PALAZZO DEI CONGRESSI
Radioterapia Oncologica: l'evoluzione al servizio dei pazienti
Associazione Italiana
Radioterapia e Oncologia clinica