Associazione Italiana Radioterapia e Oncologia clinica

Società Italiana di Radiobiologia

Upfront stereotactic radiotherapy with Cyberknife for HER2+ breast cancer patients: update of monoistitutional experience with 82 metachronous brain metastases

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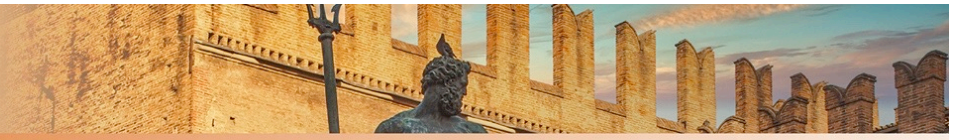

IEO Istituto Europeo di Oncologia

UNIVERSITÀ DEGLI STUDI DI MILANO

DICHIARAZIONE

Relatore: Dott. Luca Bergamaschi

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)**
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- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Altro

BACKGROUND

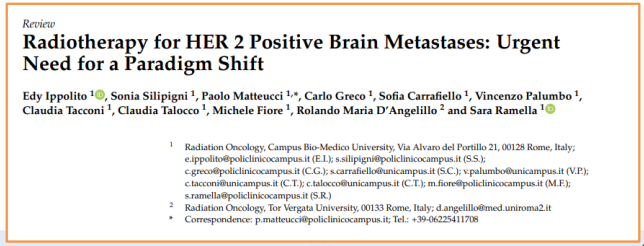
In the **HER2+** subtype of breast cancer, almost 50% of patients with metastatic disease develop **brain metastases (BM)** during their illness

Interactions between and signaling from HER2 and its family members (EGFR and HER3), have been implicated as driving factors in BM as it may drive BM through the release of matrix metalloproteases that can disrupt the blood-brain barrier (BBB).

Trastuzumab has poor penetration of the BBB, leaving the brain vulnerable to metastatic relapse, though newer generation HER2-targeting agents may circumvent these issue

In this scenario, ***intracranial control*** **may be improved with** ***local therapies***

In the last few years, because of the absence of a demonstrated survival benefit associated with the addition of WBRT, there has been a treatment paradigm shift in favour of **initial treatment with SRS**



Review

Radiotherapy for HER 2 Positive Brain Metastases: Urgent Need for a Paradigm Shift

Edy Ippolito [1], Sonia Silipigni [1], Paolo Matteucci [1,*], Carlo Greco [1], Sofia Carrafiello [1], Vincenzo Palumbo [1], Claudia Tacconi [1], Claudia Talocco [1], Michele Fiore [1], Rolando Maria D'Angelillo [2] and Sara Ramella [1]

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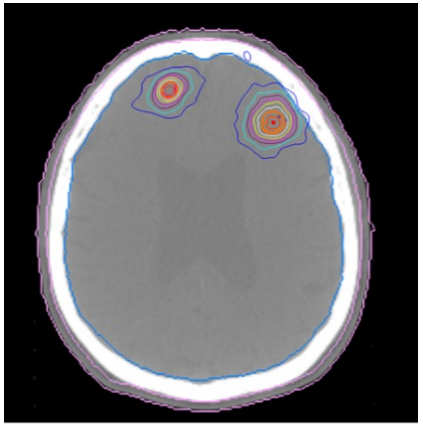
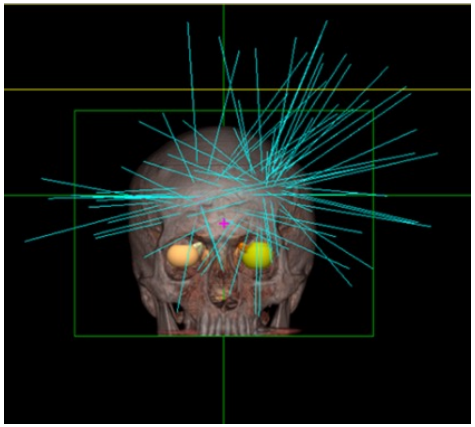
AIM OF THE STUDY

To retrospectively review our experience in a well selected population of HER2+BC patients receiving upfront SRS with Cyberknife for metachronous BM in order to explore:

- local control (LC)
- overall survival (OS)
- intra- and extracranial control





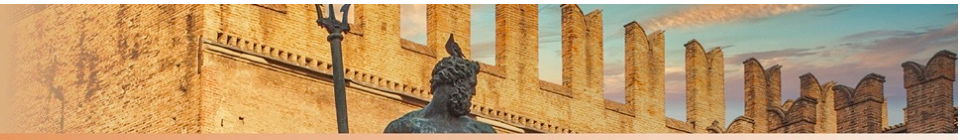
METHODS

Patients:
- Consecutive patients affected by BM from HER2+ BC receiving upfront SRS with CyberKnife (Accuray, USA)
- No previous brain treatment (such as RT or surgery)
- Written informed consent for the anonymized data for research and educational purpose.

Period: February 2012-November 2020.

Analysis: Parameters as demographics, histology and primary tumour characteristics, presence and control of extracranial disease, systemic treatment, modified breast GPA, number of lesions, single and total GTV were collected. LC, OS, progression in brain (in field and out-field), extracranial progression disease and factors related were evaluated (Kaplan Meyer).

Follow-up: CT/PET/MRI imaging was used at the discretion of the treating physician, every 3 months or sooner in case of neurologic symptoms.



RESULTS (1)

Patients

32 pts → 82 BM

Median of 2 BM for each pt (range 1-9)

Median age at the time of Cyberknife: 54 y (range 37-73)

28 pts with extracranial disease at the time of Cyberknife (controlled:19; not controlled: 9)

18 pts Luminal B/Her2+; 14 Her2+

Treatment

Median total dose: 21 Gy (range 15-24) in 1 to 3 fractions, in alternate days

Median single lesion GTV: 0.29 cm3 (range 0.02-13.22)
Median total GTV: 1.14 cm3 (range 0.11-14.08)

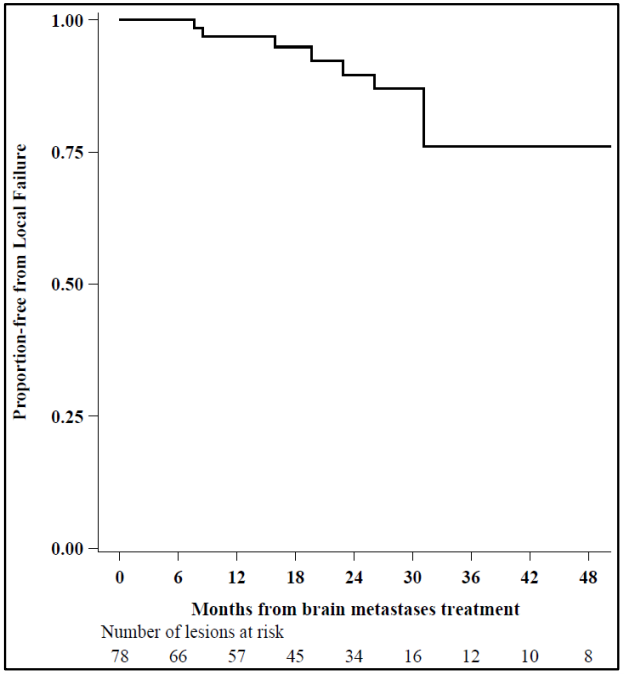
Systemic therapy*
Trastuzumab 100%
Pertuzumab 41%
Lapatinib 53%
TDM-1 69%

* previous, concomitant or subsequent

RESULTS (2)

LOCAL CONTROL (no PD in field) and INTRA-CRANIAL CONTROL*

78 BM with median follow-up of 19 months (range, 12-44)



no PD in field for 69/78 of the treated lesions (88%)

12- and 24-mo progression free from local failure of 97% (range 88-99) and 90% (range 76-96), respectively

6 of 28 patients (21%) had intra-cranial control

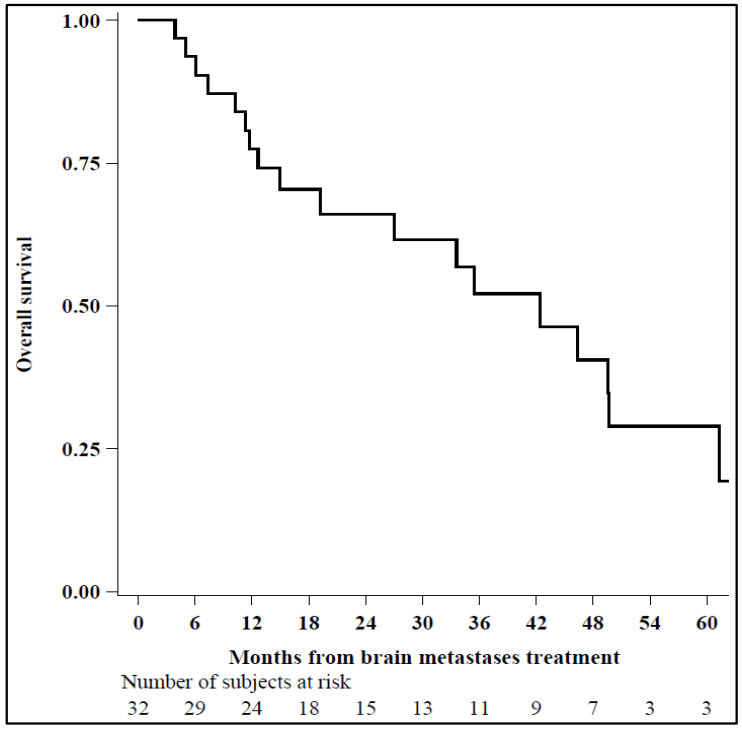
12- and 24- mo proportion-free from progression in the brain of 47% (range 28-65) and 21% (range 7-40), respectively.

Univariate analyses failed to identify any factor significantly associated with better LC

(*no appearance of any new intracranial lesions after treatment and no local recurrence of the treated lesion)

RESULTS (3)

OVERALL SURVIVAL



12- and 24-mo OS of 78% (59-89) and 66% (46-80), respectively

Among 19 deaths:

3 pts with brain disease,
4 pts with systemic disease,
11 pts with brain and systemic disease,
1 missing

Univariate analyses of OS showed that uncontrolled systemic disease at the time of SRS, was significantly negatively correlated with OS

DISCUSSION (1)

Comparison among studies are difficult because of….

Different population (studies including different biologies)

No data about RT (type, dose, volume ecc..)

Different fractionation

Different systemic therapies

DISCUSSION (2)

Small (**32 PTS**, **82 LESIONS**), but probably the largest well selected population (HER2+ and NO PREVIOUS BRAIN TREATMENT) treated with SRS

Neuro-Oncology
21(5), 659–668, 2019 | doi:10.1093/neuonc/noz006 | Advance Access date 6 February 2019

Stereotactic radiosurgery with concurrent HER2-directed therapy is associated with improved objective response for breast cancer brain metastasis

Joseph M. Kim, Jacob A. Miller, Rupesh Kotecha, Samuel T. Chao, Manmeet S. Ahluwalia, David M. Peereboom, Alireza M. Mohammadi, Gene H. Barnett, Erin S. Murphy, Michael A. Vogelbaum, Lilyana Angelov, Jame Abraham, Halle Moore, G. Thomas Budd, and John H. Suh

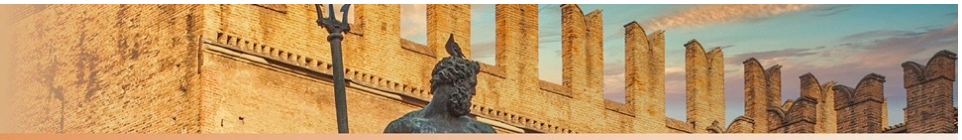
WBRT with SRS boost	39 (8)
WBRT prior to SRS	292 (60)
Surgery with SRS boost	6 (1)
Surgery prior to SRS	71 (15)

487 BM→ **79 BM** received no previous brain treatment

Stereotactic radiosurgery with concurrent lapatinib is associated with improved local control for HER2-positive breast cancer brain metastases

Shireen Parsai, MD,[1] Jacob A. Miller, MD,[2] Aditya Juloori, MD,[1] Samuel T. Chao, MD,[1,3,4] Rupesh Kotecha, MD,[5,6] Alireza M. Mohammadi, MD,[3,4,7] Manmeet S. Ahluwalia, MD,[1,3,8] Erin S. Murphy, MD,[1,3,4] Gene H. Barnett, MD, MBA,[3,4,7] Michael A. Vogelbaum, MD, PhD,[3,4,7] Lilyana Angelov, MD,[3,4,7] David M. Peereboom, MD,[1,3,8] and John H. Suh, MD[1,3,4]

Prior CNS radiation, n (%)	
WBRT	90 (71)
SRS	26 (21)
Both WBRT & SRS	24 (19)
Prior surgery, n (%)	28 (22)



DISCUSSION (3)

STRENGHT

At our knowledge, the *largest population* of HER2+ pts with no previous brain treatment, receiving SRS for BM

Excellent LC:12- and 24-mo progression free from local failure of 97% (range 88-99) and 90%

OS in line with literature

LIMITATION

Retrospective study

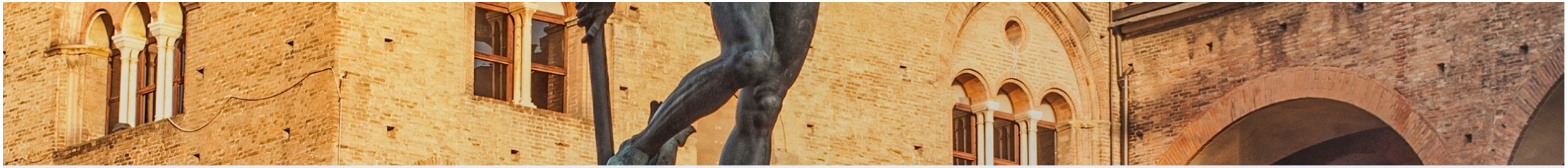
No subanalyses because of the number of the pts (i.e. OS and systemic treatment (yes/no); OS and extracranial disease (controlled/uncontrolled))

FUTURE DEVELOPMENTS

Maybe the therapeutic algorithm should be reshaped (see Ippolito et al. https://doi.org/10.3390/cancers14061514)

Prospective trials

Thank you



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