

2nd Annual Southern California Genitourinary Cancer Research Forum

Building a Successful GU Clinical & Translational Program

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IRCCS San Raffaele Hospital, Milan, Italy

Disclosures

- Grant/Research Support from AstraZeneca, BMS, Gilead Sciences, and Merck.
- Consultant for Astellas, BMS, Catalym, Daiichi Sankyo, Genenta Science, Gilead Sciences, Johnson & Johnson, Merck, and Pfizer.

This presentation and/or comments will be free of any bias toward or promotion of the above referenced companies or their product(s) and/or other business interests.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

This presentation has been peer-reviewed and no conflicts were noted.

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

This presentation is dedicated solely to research or other issues that do not contain a direct patient care component.

A note of caution

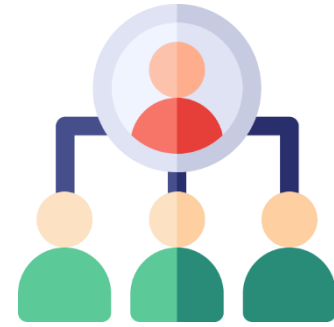
- The definition of ‘success’ is mostly subjective and based on individual goals (my personal advice does not necessarily agree with the title of my presentation)
- The content of this presentation is mostly based on my personal experience, that does not necessarily applies to a worldwide perspective
- My aim is to simply to provide you with a sincere glimpse into the journey of my life

Success is less overwhelming and shorter lasting than failure. Failure challenges who we are. It rattles our sense of being (Andrè Agassi – Open)

The importance of the cultural environment

CANCER CENTER ORGANIZATION

23 DISEASE UNITS



- Pancreatic Cancer
- CNS tumors
- Liver Unit
- NETs
- Gastroesophageal cancer
- Colorectal cancer

- Breast Unit
- Thoracic tumors
- Gynecological tumors
- Melanoma
- Thyroid carcinoma
- Molecular Tumor board
- ORL

- Leukemia Unit
- Mieloma Unit
- Myeloproliferative Neoplasm Unit
- Lymphoma Unit
- Strategic Research Program on CLL
- Allo-BMT Unit

- Prostate Cancer
- Kidney Cancer
- Bladder and Urinary tract cancer
- Rare genito-urinary tumors



I.R.C.C.S. Ospedale
San Raffaele
Gruppo San Donato

Urologic Oncology Leadership at large



Francesco Montorsi
Chair Dept of Urology
Editor Emeritus European Urology



Alberto Briganti
EiC European Urology



Umberto Capitanio
Exec. Member EAU Kidney Cancer Guidelines



Andrea Necchi
Head of GU Oncology
Ass. Ed. JCO



Arturo Chiti
Chair Dept of Nuclear Medicine
Former EiC JNMMI



Francesco De Cobelli
Chair Dept of Radiology

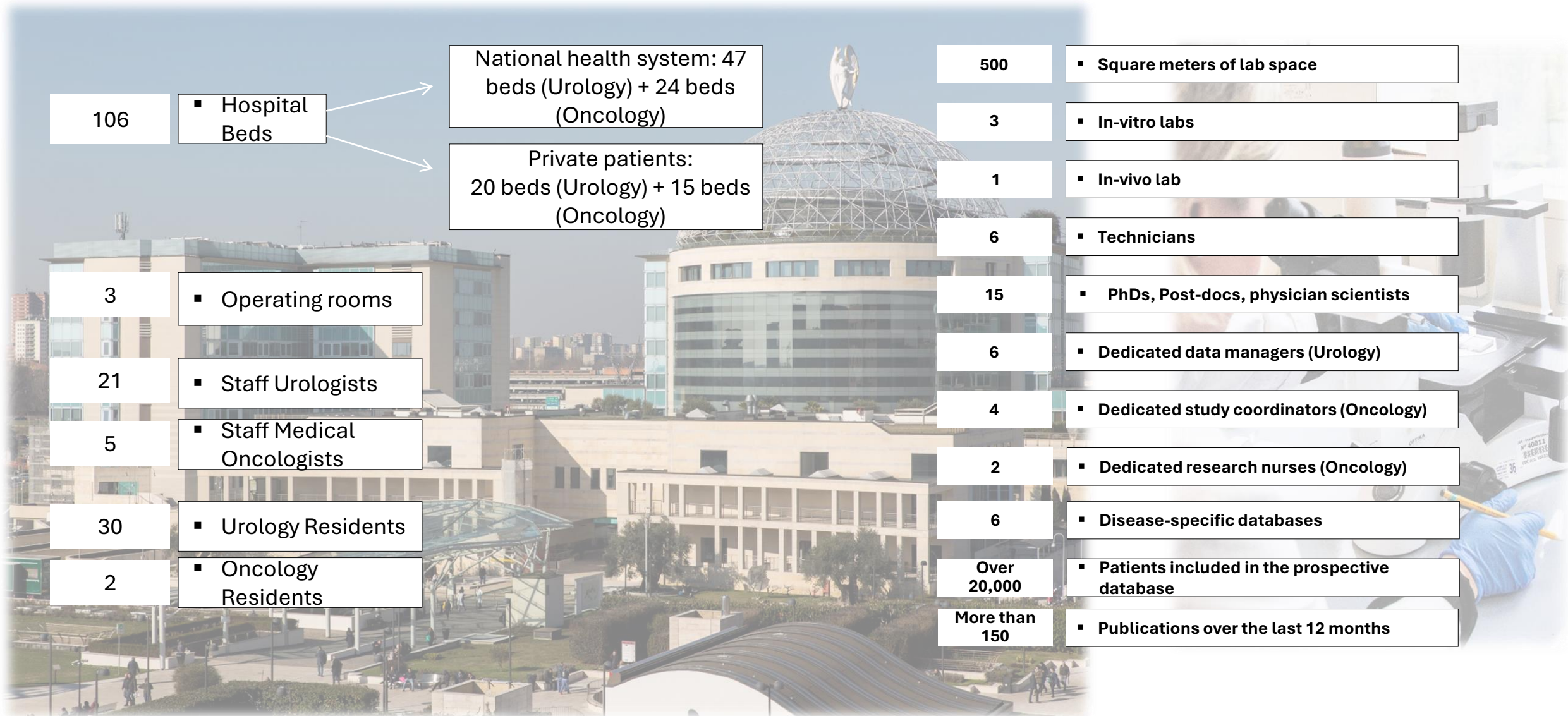


Nadia Di Muzio
Chair Dept of Radiation Oncology

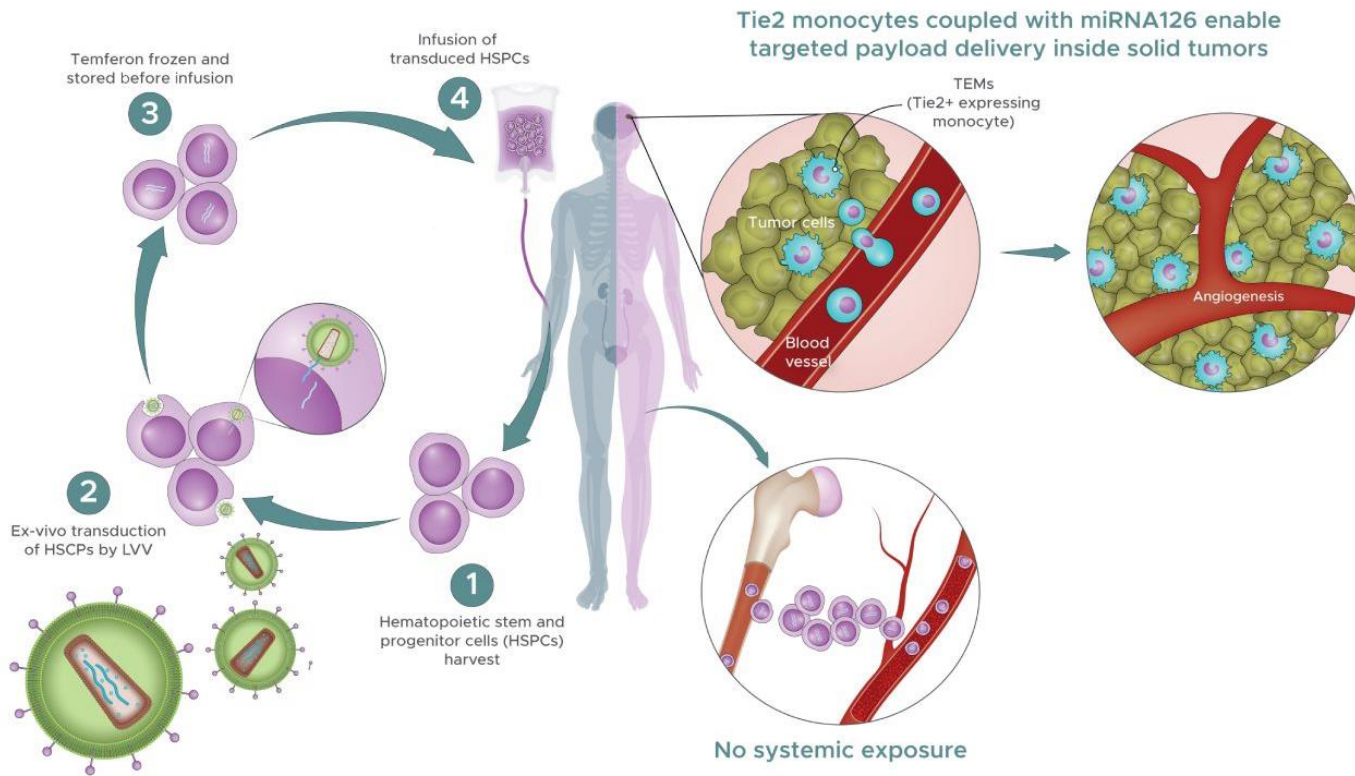


Maurizio Colecchia
Chair of ESUP (EAU Section of Urologic Pathology)

GU Oncology at large and Urological Research Institute



Clinical development of Temferon in solid tumors



TEMPERON AT A GLANCE

TEMPERON

Frozen autologous hematopoietic stem & progenitor cells (CD34+) transduced ex-vivo with a third generation LRV to drive myeloid-specific IFN- α 2 expression.

FORMULATION

Cryopreserved intravenous injectable solution.

DURABILITY OF RESPONSE

Potentially life-long.

INDICATIONS

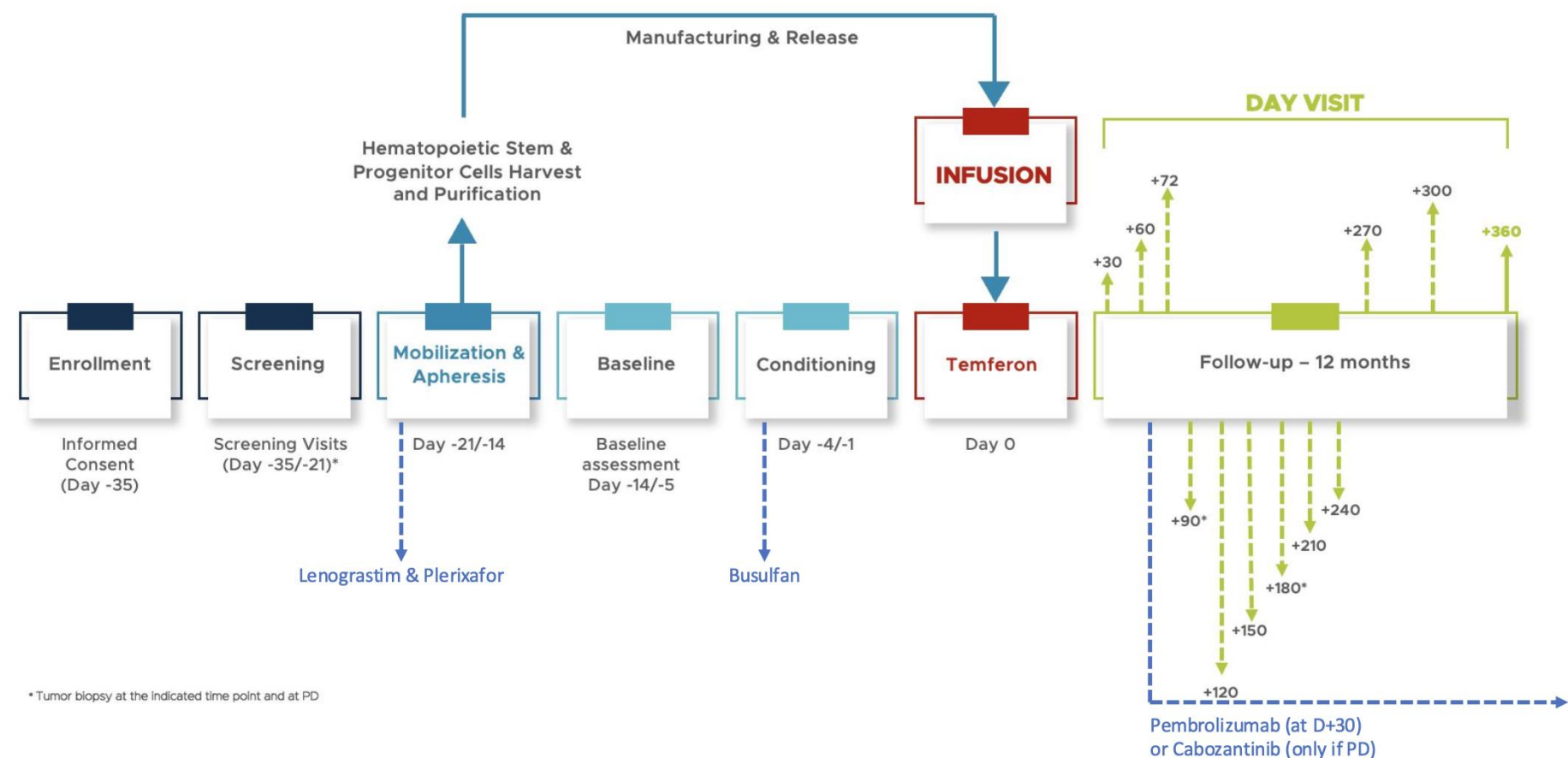
Solid tumors: uMGMT GBM & mRCC.

MECHANISM OF ACTION

Direct: anti-proliferative, anti-angiogenic;
Indirect: immune system re-programming, CD8+ T cells recruitment, T cells exhaustion counteraction.



TEM-GU: Study Procedures, NCT06716853



Pembrolizumab	400mg IV	At D+30 every 6 weeks until PD
Cabozantinib	40mg QD	In case of PD at D+30 or al later FU

Study Sponsor: Genenta Science Inc.

Recruit the Right People:

Carefully select team members based on their expertise, skills, and compatibility with the team culture. Diversify the team in terms of skills and backgrounds to encourage a wide range of perspectives and ideas

Genitourinary Oncology Unit

The 'core business' staff



- Established since Q1 2021
- Currently composed by:
 - 5 staff medical oncologists
 - 2 medical oncology residents
 - (2 PhD candidates)
 - 4 Clinical Research Coordinators
 - 2 Research Nurses



Genitourinary Oncology Unit

2024 Achievements of MD Students

ESMO COURSES IN MEDICAL
ONCOLOGY FOR MEDICAL
STUDENTS



Anna Fosfuri,
International MD Program (IMDP),
Vita-Salute San Raffaele University

Circulating immuno-biomarkers of response to neoadjuvant nivolumab and nab-paclitaxel in patients with muscle-invasive urothelial bladder cancer (MIBC): secondary analyses from NureCombo trial

ASCO 2024; NIBIT 2024



Giovanni Pastorino,
Studente V anno, Corso di Laurea in
Medicina, Università Vita-Salute



The spectrum of cutaneous toxicities related to novel genitourinary cancer therapies

Rachel Daher^{a,*}, Andrew Ruplin^b, Shilpa Gupta^c, Philippe E. Spiess^d, Ashish M. Kamat^e, Antonio Cigliola^f, Valentina Tateo^g, Chiara Mercinelli^h, Petros Grivas^b, Andrea Necchi^{a,f}

Daher R, et al. Crit Rev Oncol Hematol. 2024 Aug;200:104420



Rachel Daher,
International MD Program (IMDP),
Vita-Salute San Raffaele University

Genitourinary Oncology Unit

*Our commitment to
mentorship*

ESMO Clinical Research Fellows

- Tiago Costa de Padua (Brazil, 2021)
- Mariam Chkheidze (Georgia, 2024)



ASCO Virtual Mentorship Program (VMP)

- Christian Agbo (Nigeria, 2023)
- Tinatin Alaverdashvili (Georgia, 2024)



Other ASCO mentees (2024):

- Giulia Petrone, St. Louis, USA
- Anne-Christine Buteau, NY, USA
- Gayatri Narayan, Los Angeles, USA

Partnering with multiple departments within a clinical trial

The PURE-01 legacy



Filippo Pederzoli

Stool Microbiota Profiling

2021 ASCO Annual Meeting

Conquer Cancer Foundation of ASCO Merit Award Recipient

[Pederzoli F, et al. *Eur Urol.* 2024 May;85\(5\):417-421.](#)

Antibiotic use and outcome of neoadjuvant pembrolizumab in PURE-01

[Pederzoli F, et al. *Eur Urol.* 2021 Sep;80\(3\):319-322.](#)



Giuseppe Basile

Updated PURE-01 results

2023 EAU Best Paper in Clinical Research

[Basile G, et al. *Clin Cancer Res.* 2022 Dec 1;28\(23\):5107-5114.](#)



Giorgio Brembilla

VI-RADS and pathological response prediction after neoadjuvant pembrolizumab

2023 GU Cancers Symposium

Conquer Cancer Foundation of ASCO Merit Award Recipient 2023

[Brembilla G, et al. *Radiology.* 2024 Dec;313\(3\):e233020.](#)



Valentina Tateo

ER signature expression and response to neoadjuvant pembrolizumab in MIBC

2024 Genitourinary Cancers Symposium

Merit Award Recipient

[Tateo V, et al. *Paper in press*](#)

Fulfilling Your Goals



UniSR
Università Vita-Salute
San Raffaele



I.R.C.C.S. Ospedale
San Raffaele
Gruppo San Donato



2010
Urology Unit
Fondazione IRCCS Istituto Nazionale dei Tumori, Milan



Protocollo 0001



ISTITUTO NAZIONALE
PER LO STUDIO
E LA CURA DEI TUMORI

Partecipanti: G. Bonadonna, E. Lorfardini,
E. De Lena, F. Ponzetti-Bela-
iani, G. Leratta, E. Saffa-
ta.

Luglio 1970

Atto: Roma - 44 settembre 1970 - 10.10.1970 - 10.10.1970 - 10.10.1970

Somministrazione di adriamicina in tumori solidi mediante
un nuovo schema terapeutico.

A) SCOPO: Determinare (con il N.C.C.S.C.) la tossicità e l'efficacia dell'adriamicina in vari tumori solidi dell'adulto e dell'infanzia mediante un nuovo schema terapeutico intermittente.

B) SCELTA DEI PAZIENTI: sono candidati tutti i pazienti con linfoma o neoplasia solida in fase avanzata. Sono esclusi i casi trattati con chemioterapie nelle tre settimane precedenti la somministrazione dell'adriamicina, i casi con riserva mielolare compromessa, con ipertensione e con anamnesi di malattie coronariche e aritmia cardiaca.

C) ESAMI DI LABORATORIO: emocritia completa, creatinemia, uricemia, SGOT, SGPT, fosfatasi alcalina, BuF, elettroforasi, XG, CPK; ove possibile, mielogramma. L'emocritia va ripetuta 2-3 volte la settimana (con particolare attenzione attorno al 14° giorno), mentre gli altri esami verranno ripetuti prima di ogni ciclo terapeutico.

D) DOSE PIENA: 25 mg/m²/die x 3 i.v. (G.B. 5000; PP 150.000)

DOSE RIDOTTA: 20 mg/m²/die x 3 i.v. (G.B. 3-5000; PP 100-150.000)

Il dosaggio può essere modificato nel tempo usando le seguenti dosi in base ai valori minimi dell'emocritia ottenuti nelle tre settimane di intervallo:

dose iniziale
piena
ridotta

G.B.	PP	Dose seguente
5000	150000	aumentare di un livello
3-5000	100-150000	invariata
2-3000	50-100000	diminuire di un livello
2000	50000	diminuire di due livelli

G.B.	PP	Dose seguente
3-5000	100-150000	aumentare di un livello
2-3000	50-100000	invariata
2000	50000	diminuire di un livello

E) DURATA DEL TRATTAMENTO: se vi è risposta obiettiva, proseguire ogni tre settimane fino alla ripresa della neoplasia. Se vi è arresto della crescita della neoplasia, la terapia può essere proseguita a discrezione del ricercatore. Se vi è progressione della malattia, il trattamento viene proseguito fino a produrre mielodepressione. Se il tumore a questo punto continua a proliferare il trattamento viene interrotto.

Il trattamento viene considerato superato se l'adriamicina viene somministrata per un minimo di due cicli. Per ogni tipo istologico è necessario trattare 15 pazienti in modo adeguato per poter determinare una risposta terapeutica del 50% o più.

UniSR

Set up a Supportive Infrastructure (clinical trials machinery):

Provide the necessary tools, technology, and resources that the team needs to perform their tasks efficiently

Having a brilliant idea

STEP #1 (Individual value)

Getting funded to develop the idea

STEP #2 (Strategy)

Setting the proper stage to the study

STEP #3 (Business)

Pursue the original aim until the study conclusion

STEP #3 (Resilience)



Hurdles in developing investigator-initiated clinical trials



Primary sources of budget affording our clinical/translational research and team members salary (Years 2021-2024)

 Grants from approved investigator-initiated clinical trials:

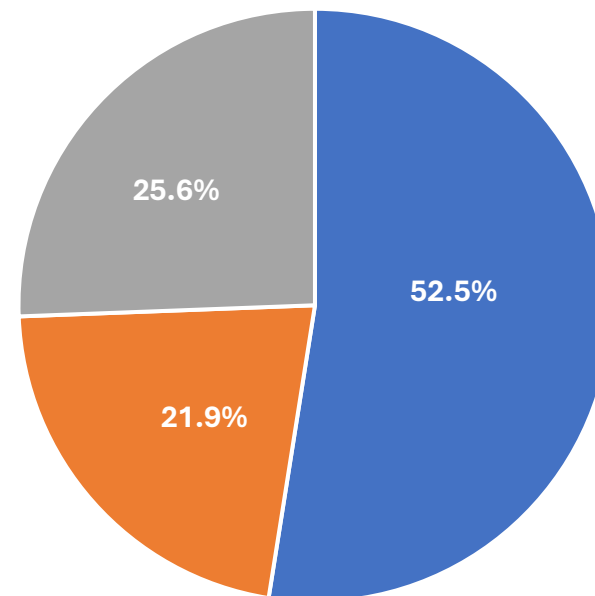
- 760,626.34 € (SURE-01, SURE-02, NureCombo)

 Grants from academic funding sources/calls:

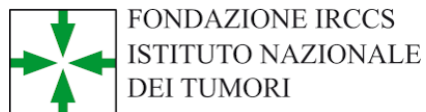
- 645,000.00 € (AIRC Investigator Grant)

 Income from Pharma-Sponsored clinical trials:

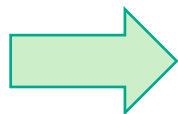
- 1,554,585.35 €



Primary sources of budget affording a clinical investigator career



GlaxoSmithKline Inc.



Articles



Pazopanib in advanced and platinum-resistant urothelial cancer: an open-label, single group, phase 2 trial

Andrea Necchi, Luigi Mariani, Nadia Zaffaroni, Lawrence H Schwartz, Patrizia Giannatempo, Flavio Crippa, Carlo Morosi, Rodolfo Lanocita, Teodoro Sava, Cinzia Ortega, Caterina Messina, Cosimo Sacco, Marzia Pennati, Maria G Daidone, Nicola Nicolai, Filippo De Braud, Alessandro M Gianni, Roberto Salvioni

Value of industrial partnership and vision

Necchi A, et al. *Lancet Oncol.* 2012 Aug;13(8):810-6

Primary sources of budget affording a clinical investigator career



MyFirst AIRC Grant (2016-2020): *Insights into the activity of immune-checkpoint inhibitors in patients with muscle-invasive urothelial bladder cancer*

AIRC Investigator Grant (2022-2027): *Understanding tumor and immune dynamics and predicting response to various perioperative therapies in patients with MIBC*

2023 “Beppe della Porta” Award



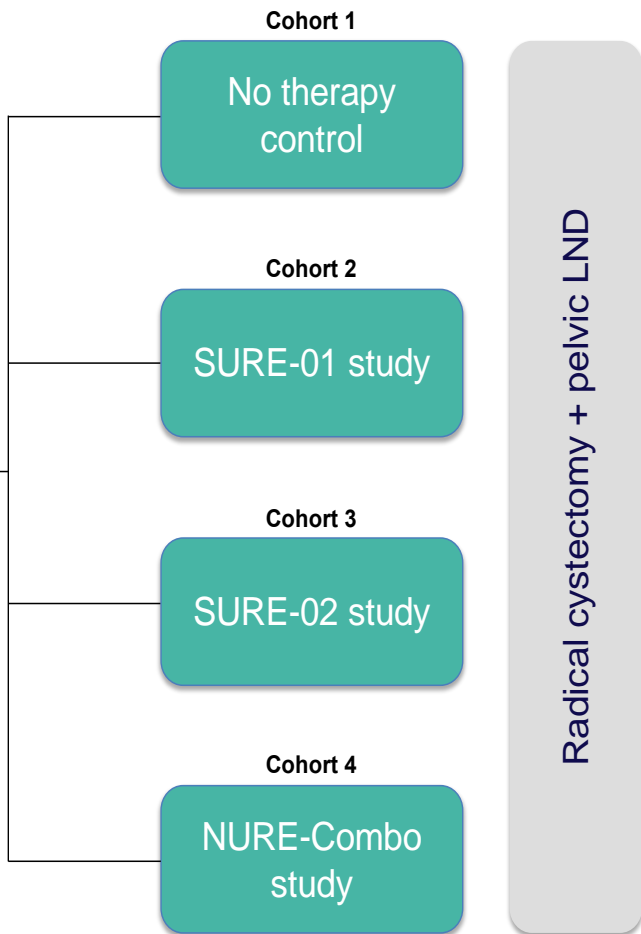
Research Projects

Understanding tumor and immune dynamics and predicting response to various perioperative therapies in patients with MIBC: AIRC IG 2023 (€ 645.000,00)



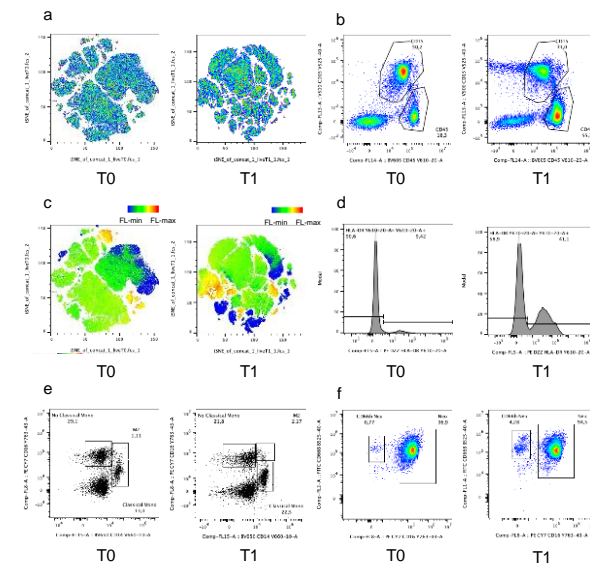
PATIENT POPULATION

- Histologically confirmed MIBC with predominant urothelial histology
- Clinical stage T2-4N0M0
- Cisplatin-ineligible MIBC
- No prior systemic anti-neoplastic treatment for MIBC
- Eligible for radical cystectomy and pelvic lymph node dissection
- Received TURBT
- ECOG performance status 0, 1



Whole transcriptome expression analyses (Veracyte Inc.)

Immune-monitoring by multiparametric flow cytometry



Multiplex immunofluorescence and spatial distribution of immune populations (University of Padua, Italy)

Noninvasive prediction of tumor response to neoadjuvant treatment: PET/MRI & VI-RADS (in partnership with MSK Radiology)

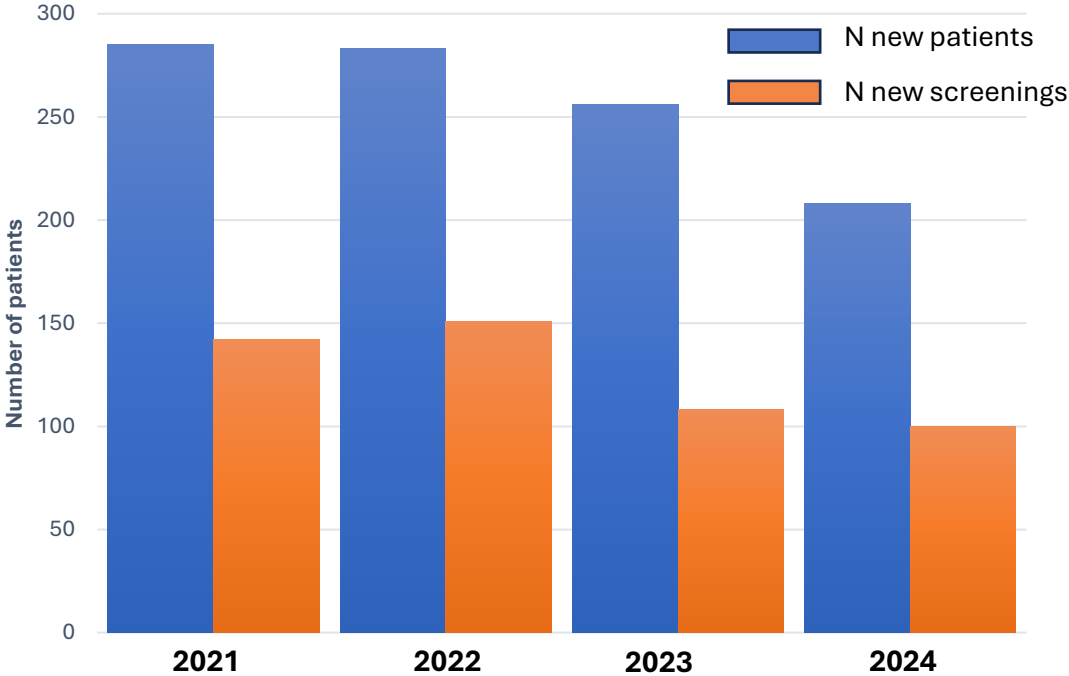


Outline of clinical trials activity at GU Medical Oncology Unit at San Raffaele Hospital (Years 2021-2024)*

- Average % of patients screened for clinical trials: 50%
- Currently, 46 trials are offered at our Unit.

Tumor type	Active trials	Open to accrual
Prostate Cancer	8	4
Urothelial carcinoma	30*	20
Renal cell carcinoma	7	4
Tumor agnostic/rare GU tumors	1	1

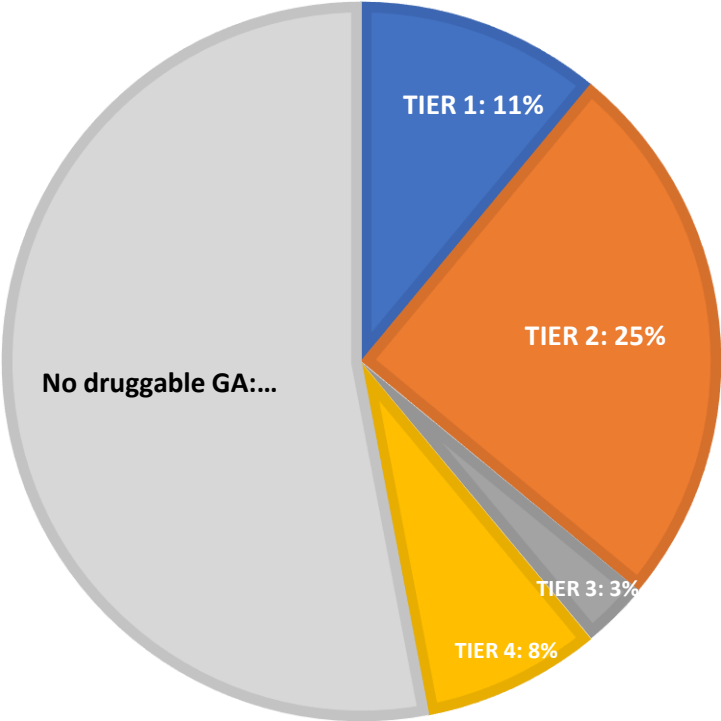
*GU Oncology is also an independent Phase 1 Unit within the Department of Medical Oncology



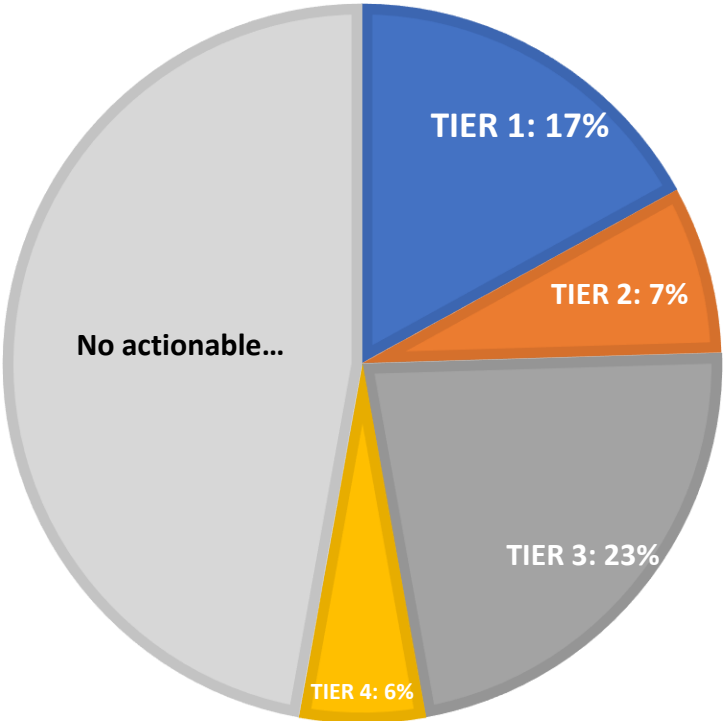
Establish clear roles and responsibilities: Define the roles and responsibilities of each team member to avoid confusion and overlap. This clarity helps team members understand their contributions and enhances accountability

Outline of 2022 Activity from the Clinical-Genomic Database: GU Medical Oncology Unit at San Raffaele Hospital

ESCAT Prostate Cancer (N=100)



ESCAT Bladder Urothelial Carcinoma (N=53)

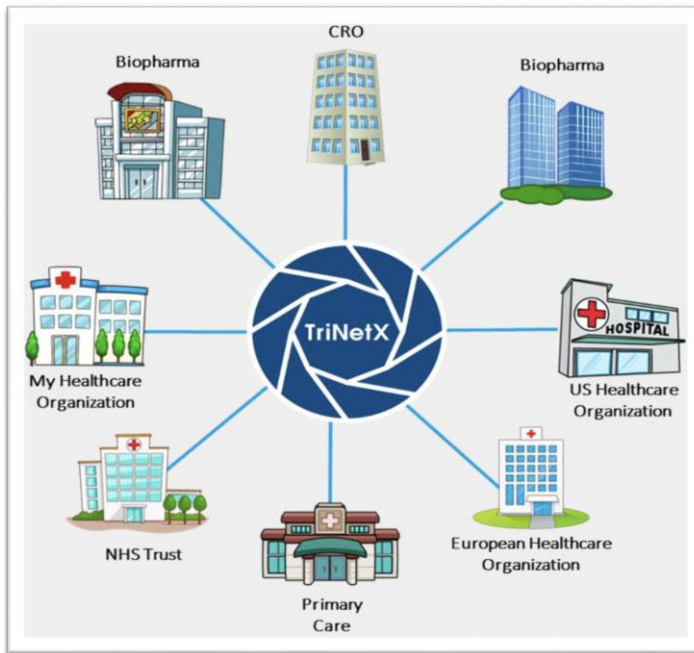


- Legend:**
- ERBB2 SV mutations considered TIER III based on recent US FDA approval of trastuzumab deruxtecan for ERBB2 mutated (not amplified) NSCLC
 - PIK3CA SV mutations considered TIER II (can be TIER V in endocrine cancers where ER+ is required for co-targeting)
 - ERBB3 SV mutations or amplification consider TIER IV in bladder
 - ATM SV mutations in prostate considered TIER I (PARPi) but will likely be changed by US FDA soon

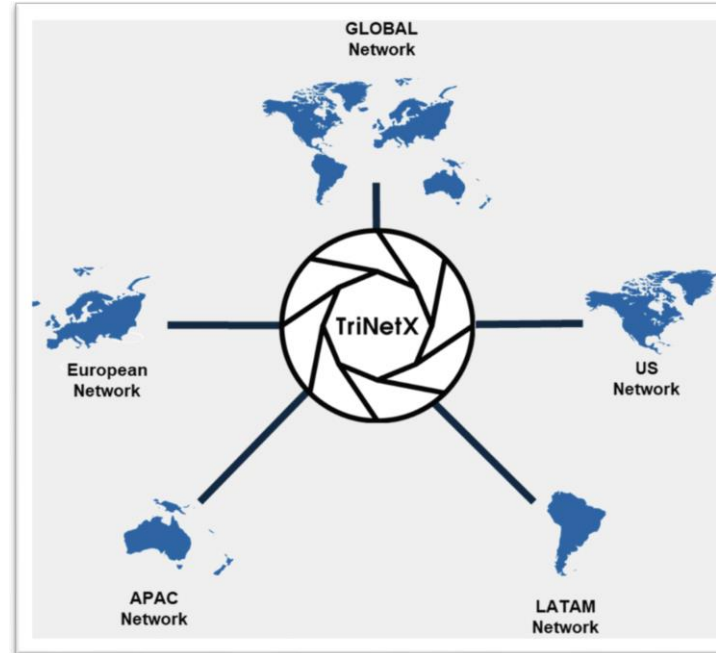


- Federated network, control over data remains in hospital
- Real-time access to patient populations, driven and refreshed by electronic medical record (EMR) data, to determine protocol feasibility, cohort analysis and site identification

Latest analyses:



An ecosystem of HCOs, biopharmaceutical companies and CROs to jointly improve Clinical Research



A Global footprint allowing access to large regional anonymous Data Networks to advance Real World Evidence

- **Maiorano BA, et al.**

Outcomes of immune-checkpoint inhibitor rechallenge in urothelial carcinoma: Results from a global real-world evidence study
#GU25 – J Clin Oncol 43, 2025 (suppl 5; abstr 732)

- **Maiorano BA, et al.**

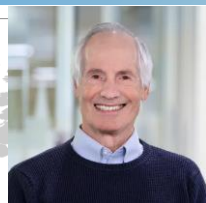
Outcomes of patients with muscle-invasive bladder carcinoma (MIBC) not receiving radical cystectomy (RC) nor radiotherapy (RT) after neoadjuvant chemotherapy: A global real-world study
#EAU25; #AUA25

- **Cigliola A, et al.**

Outcomes of immune-checkpoint inhibitors rechallenge in metastatic clear cell renal cell carcinoma: results from a global real-world evidence study
#EAU25; #AUA25

Promote Collaboration:

Foster a collaborative culture where team members feel comfortable sharing ideas and providing feedback. Utilize collaborative tools and platforms that facilitate communication and information sharing



Academic partnerships:

- MSKCC, Radiology Department:
 - *Artificial intelligence to predict the response to neoadjuvant therapies in MIBC*
- University of Padua:
 - *Using multiplex IHC to characterize response/resistance mechanisms to neoadjuvant experimental therapies in MIBC*
- Northwestern University:
 - Comprehensive molecular profiling of tumor response to various neoadjuvant therapies in MIBC

Industrial Partnerships:

- Foundation Medicine Inc.
 - *Comprehensive genomic profiling (CGP) and Real-World Clinical Outcome Data (RWCO), in partnership with Flatiron Health Inc.**
- Natera Inc.
 - *MRD monitoring in patients with MIBC undergoing experimental perioperative therapies.*
- Veracyte Inc.
 - *Whole transcriptome sequencing of matched pre-post therapy samples from MIBC undergoing experimental perioperative therapies*
- Genenta Sciences Inc. (TEMS GU Program)

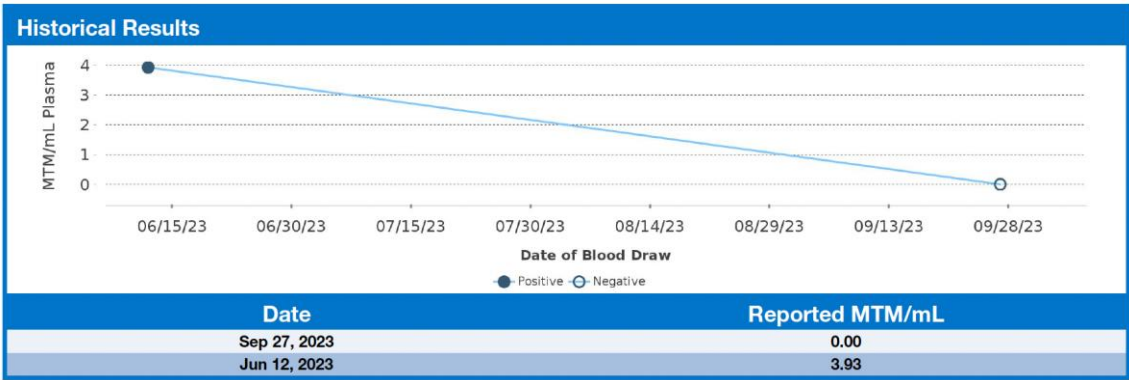
Established international collaborations in GU oncology at San Raffaele Hospital since 2021

Encourage Innovation and Creativity:

Create an environment where team members feel encouraged to think creatively and innovate. This involves being open to new ideas and taking calculated risks.

NureCombo trial: neoadjuvant Nivolumab + Nab-paclitaxel > RC > adjuvant nivolumab (NCT04876313)¹

June 2023) **Case ID#31:** 69 yo, Male; cT3N0 Urothelial Carcinoma



ctDNA monitoring

Nivo/ABX x 4 cycles

TURBT



RC refusal



reTURBT: ypT0

Adjuvant Nivo




MRI
CT
PET



MRI
CT
PET

**Radiological CR
VI-RADS=0**

1. Mercinelli C, et al. *J Clin Oncol*. 2024 Dec 10;42(35):4196-4205



Transmitting a True Sense of Mission
We all want to feel we are a part of something bigger

Genitourinary Oncology Unit

*The GU Oncology
Retreat Legacy*



2022



2023



2024



Joint Summit of International Bladder Cancer Group (IBCG)
& the Global Society of Rare Genitourinary Tumors (GSRGT)

**DEFINING NEW ENDPOINTS AND DESIGN OF NEXT-GENERATION
TRIALS OF PERIOPERATIVE THERAPIES IN MUSCLE-INVASIVE BLADDER CANCER**

DECEMBER 14th, 2024

2022



2024





Highlights from the GSRGT



HISTORICAL PERSPECTIVE

1

July 2020

Phil Spiess and myself discussed the creation of a Rare GU Tumors society

2

July-September

Formal creation of the GSRGT including charter and bylaw development and implementation of a leadership

3

September 3, 2020

Our first board meeting took place with some of the worlds most profound leadership

4

December 11-12, 2020

The first Global Summit for the GSRGT took place including 24 speakers and over 500+ guests



PRESIDENT

Philippe E. Spiess, M.D., MS, FRCS(C), FACS
Senior Member, Dept of GU Oncology
Senior Member, Dept of Tumor Biology
Assistant Chief of Surgical Services
Moffitt Cancer Center
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University of South Florida



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Urology - Urology Oncology - Robotic and
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General Hospital
Urology Associates of Rochester
Rochester - New York



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Professor of Clinical Trials, Director of the
Southampton Clinical Trials Unit



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Clinical Program Director of Genitourinary
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at Virginia Commonwealth University



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Hassan II University Hospital,
Morocco, Fes

LEADERSHIP cOUNCIL

Penile cancer endeavor



Giuliano AR, et al. *N Engl J Med*. 2011





GLOBAL SOCIETY OF
RARE GENITOURINARY TUMORS

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GSRGT _____

International society of scientists, experts and patient advocates committed to improving the care of rare GU tumors through science and education.

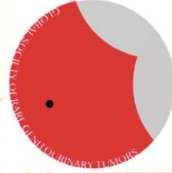
gsrgt.org

IMPORTANT GLOBAL PARTNERSHIP BETWEEN THE IBCG and GSRGT



INTERNATIONAL
**BLADDER CANCER
GROUP**

- Official partnership was established in December 2022 and facilitated by Professor Ashish Kamat
- Joint committee led by Drs Roger Li and Shilpa Gupta, with several global ambassadors
- First joint meeting held at IBCG meeting in Houston, Texas on August 25th-26th, 2023
- Focus on advancing the care of patients impacted with urothelial carcinoma of variant histologies and also developing evidence-based consensus guidelines



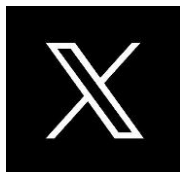
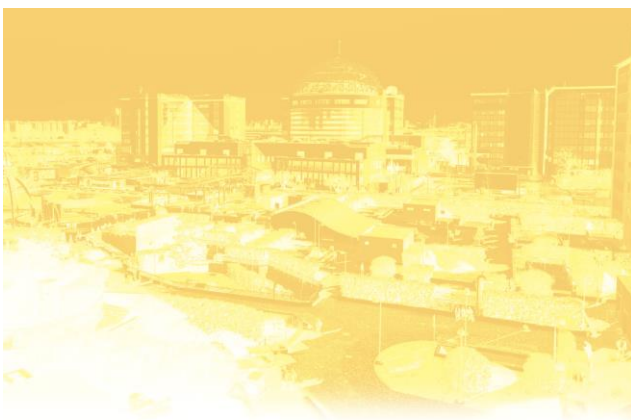
INTERNATIONAL
BLADDER CANCER
GROUP

Joint Summit of International Bladder Cancer Group (IBCG) & the Global Society of Rare Genitourinary Tumors (GSRGT)

DECEMBER 14th, 2024

Sala Convegni - HOTEL NH Milano 2 - SEGRATE [MI]

**DEFINING NEW ENDPOINTS AND DESIGN OF NEXT-GENERATION
TRIALS OF PERIOPERATIVE THERAPIES IN MUSCLE-INVASIVE BLADDER CANCER**



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@AndreaNecchi





SAN RAFFAELE
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