
2019
21-23 JUNE
SAN FRANCISCO
SUPPORTIVE CARE
MAKES EXCELLENT
CANCER CARE POSSIBLE
NICSO (Italian Network of Supportive Care in Cancer)
RESEARCH PROGRAM
MASCC/ISOO
Annual Meeting on Suppportive Care in Cancer
www.mascc.org/meeting
Follow us on Twitter: @CancerCareMASCC
MASCC
Multinational Association of Supportive Care in Cancer
ISOO
INTERNATIONAL SOCIETY of ORAL ONCOLOGY
#MASCC19

Conflict of Interest Disclosure

Paolo Bossi, MD

- Consulting Fees (e.g., advisory boards): Roche, Merck Serono, Kyowa Kirin, AstraZeneca, MSD, Angelini, SunPharma and Sanofi

Clinical trials and scientific projects by NICSO

- Mission of NICSO is developing trials and increasing knowledge about supportive care in patients during all their pathway of care

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Clinical trials and scientific projects by NICSO

- Monitoring adverse events (AE) by oncological treatments – National trial
- Defining treatment with immunotherapy (IT) in challenging populations at higher risk of AE
- Real world data from challenging pts treated with Immunotherapy

Clinical trials by NICSO

Studio Nazionale NICSO:
Progetto Di Monitoraggio Medico-Infermieristico Degli Effetti Collaterali Da Terapie Oncologiche

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PHYSICIAN AND **NURSE**-BASED STRATEGIES TO MONITOR ADVERSE EVENTS BY ONCOLOGICAL TREATMENTS

Background

- Lack of compliance to guidelines in supportive care during oncological treatments causes an increased frequency and duration of AEs

- Early discovery of AEs may offer a better approach and a reduction of severity and duration

Background

- Better management of AEs may favorably impact on respect of treatment dose-intensity

- Employing PRO measures of toxicities allow to improve sensitivity and may increase pt QoL and survival

Open questions

How to better assess and monitor toxicities induced by treatments?

Who should be in charge of evaluating toxicities?

Could we empower patients in AEs prevention?

How much the prompt evaluation of toxicities may reduce time spent with toxicities?

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Study Design

Multicenter, randomized, open label trial comparing

the use of a standard «dashboard» to guide prevention/ treatment of Tox given by the physician

vs

the same indications of the «dashboard» + a periodic empowerment of the patient through a phone call by a specialized nurse

Objectives of the study

PRIMARY:

to assess number of days with any toxicity (evaluated by PRO CTCAE) grade ≥ 3

SECONDARY:

- Incidence and duration AEs grade 1-2;
- Number of unplanned access to ER or to unplanned visits;
- Number of days spent as inpatient due to Toxicities
- Quality of life

Exploratory:

- Dose intensity of oncologic treatment

Study population

Any kind of patient with solid tumour treated for the first time with

- Adjuvant chemotherapy
- Targeted agents
- Immunotherapy

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Inclusion criteria

Adjuvant chemotherapy:

- Antracyclin + cyclofosfamide ± taxanes (Breast cancer)
- Oxaliplatin + fluoropirimidine (Colon cancer)
- Platinum based therapies (Lung cancer)

Targeted agents:

- sunutinib, pazopanib (Kidney cancer)
- gefitinib, erlotinib,afanitinib, crizotinib (Lung cancer)
- vemurafenib ± comimetinib, dabrafenib±trametinib (Melanoma)
- everolimus ± exemestame (Breast cancer)
- CKI (Breast cancer)
- Vandetanib, lenvatinib (Thyroid cancer)
- vismodegib (BCC)
- imatinib (GIST)

Immunotherapy:

- anti CTLA4
- antiPD1/PDL-1

Dashboard and Nurse phone call

- **DASHBOARD** = Informative sheet, built with the expertise of a multidisciplinary team and containing the updated guidelines for prevention and treatment of AEs due to the different treatments

- **NURSE PHONE CALL**: phone call made weekly by a group of experienced nurses, with the aim of coaching the patient and empowering him/her to recognize and treat AEs due to the therapy.

  Nurses will guide patients to choose the right action with regard to toxicities.

Tools to measure endpoints

- **PRO CTCAE**: administered to all the patients weekly, for 4-6 months
- **EORTC QLQ-C30**: administered every month
- Dose intensity assessment
- Number of unplanned visits and ER accesses measured through clinical charts

Statistical considerations

- Estimated prevalence of 15% (time spent with tox grade 3-4), with power = 0.9 and alpha = 0.05, we would like to show a reduction to 5% of the time spent with tox grade 3-4 in the experimental arm

- Sample size = 207 pts per arm in each group of treatment (1252 pts overall)

- 24 months of accrual

NICSO Centers

- 53 Centers involved in Italy
- 415 pts enrolled till now
- First results: Jan 2020

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Expectations

- To define standard of care in monitoring toxicities according to each treatment
- To prospectively describe the pattern of toxicities with PRO
- To assess the use of emergency services

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Defining treatment with immunotherapy (IT) in challenging populations at higher risk of AE

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- Immunotherapy has been approved in several indications based on the positive results of phase III trials

- However, phase III trials are not fully representative of the whole population, as several exclusion criteria exist

Challenging populations at higher risk of AE

WHO ARE THEY?

- **Elderly** pts
- Pts with underlying ***major infections*** (HBV/HCV/HIV)
- Pts with **autoimmune diseases** of any kind
- **Solid transplant** recipients
- Pts with **lymphoproliferative disease** or receiving **transplant** for hematological malignancy

Room for IT in challenging populations at higher risk of AE?

- We performed an extensive lyterature review to evaluate the existing data and to give expert opinions of a multidisciplinary group of physicians involved in care of pts with immunotherapy induced toxicities

Elderly pts

- Older adults with good performance status appear to benefit similarly to single-agent checkpoint inhibitor therapy as their younger counterparts
- Overall toxicity appears similar, but hospitalizations and influence of poor funtional status and multimorbidity in the real world remain.
- The role of a geriatric assessment for older adults receiving immunotherapies remains unclear but may be useful to gauge fitness for more intense therapies, such as combined immunotherapy, chemoimmunotherapy, or chemotherapy/radiation plus immunotherapy strategies
- More research is needed to evaluate the correlation between markers of immunosenescence among older adults receiving immunotherapy and the effect of these relationships on biological, clinical, functional, and patient-reported outcomes.

Pts with HBV infection

- Patients with active HBV infection (HBsAg pos, HBV DNA ≥2,000 IU/mL, ALT>ULN) should be put on long-term therapy with entecavir or tenofovir, until HBsAg seroconversion

- Inactive carriers of HBsAg (HBsAg pos, HBeAb pos, HBV DNA <2,000 IU/mL, ALT normal) receiving ICIs have to receive prophylaxis with lamivudine, entecavir or tenofovir, until 12-18 months after completion of ICIs, although risk of reactivation is probably low

- In patients with cured HBV infection (HBsAg neg, HBcAb pos, HBsAg pos or neg) receiving ICIs, should be monitored for HBsAg or HBV DNA without active therapy

Pts with HCV infection

- Treatment with ICIs appears to be safe in patients with chronic HCV infection
- Treatment for HCV should be offered to all patients with detectable viral load
- Safe and successful treatment in the presence of an untreated hepatitis C infection with a detectable viral load has been reported

Pts with autoimmune diseases

- ICI can induce a wide variety of rheumatic irAEs either in previously undiseased patients or in those with pre-existing autoimmune conditions
- Reports of rheumatic irAEs have been sparse and were only described in case reports or small series
- Frequency of rheumatic irAEs in previously undiseased patients is variable and arthralgias and mialgias seem the most frequent
- Frequency of rheumatic irAEs in patients already affected by rheumatic diseases who develop cancer in the course of their diseases is higher
- Severe events are rare and in most cases steroid therapy is resolutive

Real world data from challenging pts treated with Immunotherapy

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- Through Phase IV clinical studies, new drugs can be **tested continuously** to uncover more information about efficacy, safety and side effects after being approved for marketing

Phase IV trials: are necessary?

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✓ YES!

Phase I-III trial are conducted
in a **relatively limited number of patients**:

→ Therefore, when looking at rarer AEs, it is possible that they are under-reported or even not reported!

RARER ADVERSE EVENTS

- **The case of cardiotoxicity.**

The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Fulminant Myocarditis with Combination Immune Checkpoint Blockade

Douglas B. Johnson, M.D., Justin M. Balko, Pharm.D., Ph.D.,

REVIEW ARTICLE

Potential cardiac risk of immune-checkpoint blockade as anticancer treatment: What we know, what we do not know, and what we can do to prevent adverse effects

Paolo Spallarossa[1] | Giovanni Meliota[1] | Claudio Brunelli[1] |

Probl Cancer 42 (2018) 422–432

...ts lists available at ScienceDirect

Curr Probl Cancer

journal homepage: www.elsevier.com/locate/cpcancer

ELSEVIER

Cardiotoxicities associated with immune checkpoint inhibitors

Shu Yang[a], Aarti Asnani[b,*]

RARER ADVERSE EVENTS

Cardiovascular toxicities associated with immune checkpoint inhibitors: an observational, retrospective, pharmacovigilance study

Joe-Elie Salem, Ali Manouchehri, Melissa Moey, Bénédicte Lebrun-Vignes, Lisa Bastarache, Antoine Pariente, Aurélien Gobert, Jean-Philippe Spano, Justin M Balko, Marc P Bonaca, Dan M Roden, Douglas B Johnson, Javid J Moslehi

Lanc Oncol Nov 2018

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ICI→ more myocarditis, pericardial diseases, supraventricular arrhythmias, and vasculitis compared with adv events in the full database

Phase IV trial in SELECTED population

- **Opposite selection** in respect to registration trial… only specific subgroups not included (or less-included) in clinical trials

Aim: *to test the drug effect in specific populations (subpopulations)*

IMMUNOTHERAPY IN PATIENT POPULATIONS AT HIGHER RISK OF ADVERSE EVENTS

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- Observational phase 4 multicenter study, in challenging populations treated with immunotherapy per clinical practice.
- **Aim**: is to observe the rate of high-grade toxicities in this specific population. Results will be indirectly compared to what observed for “fit patients” normally represented in clinical trials.

COOPERATION IS THE KEY OF SUCCESS, ALSO IN SUPPORTIVE CARE!

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Thanks by NICSO!