



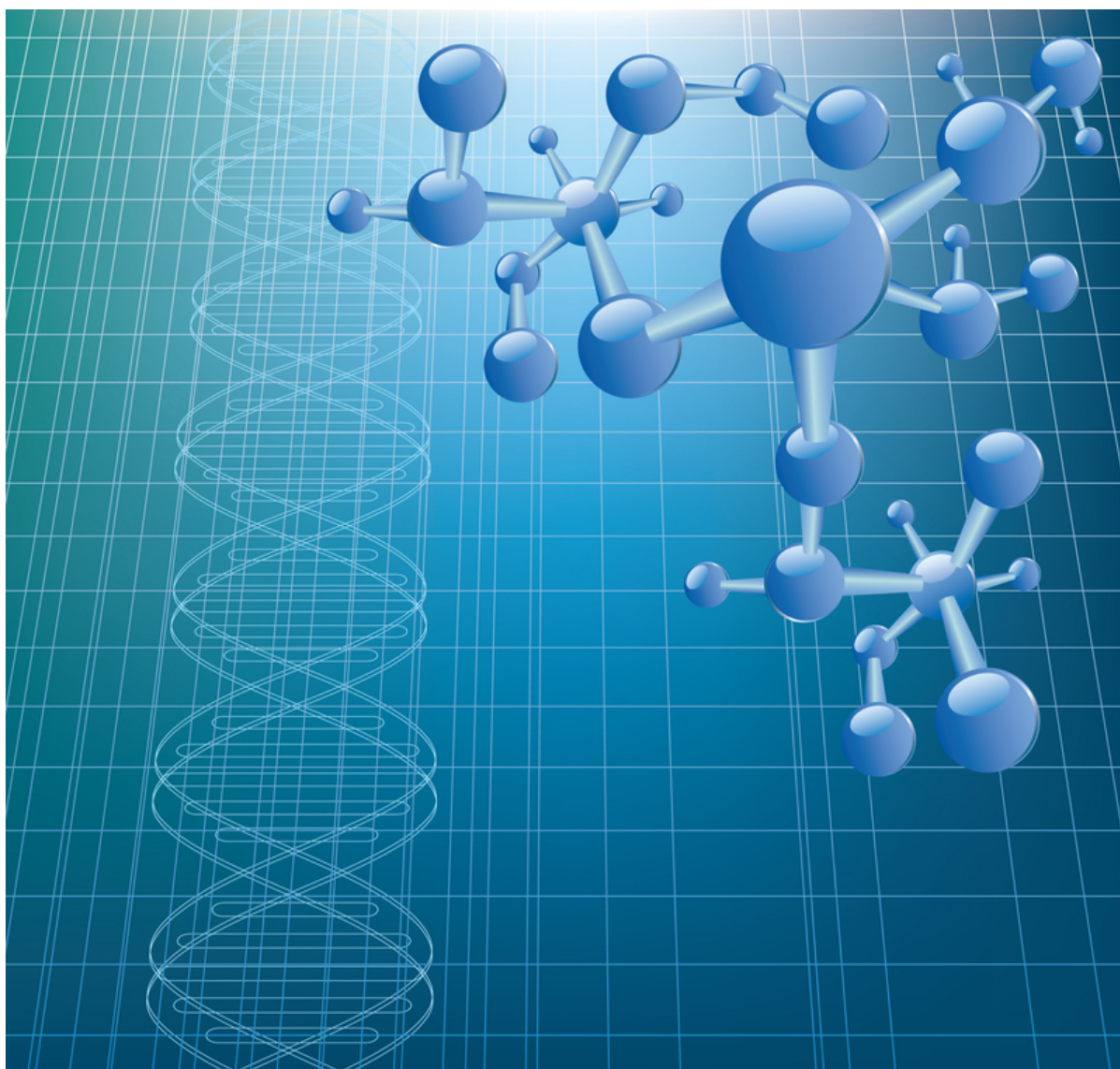
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH



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Paediatric strategy forum for medicinal product development of checkpoint inhibitors for use in combination therapy in paediatric patients

5-6 September 2018



Background and objectives

The third multi-stakeholder Paediatric Strategy Forum, jointly organised by EMA and ACCELERATE will focus on checkpoint inhibitors used in combination therapy, in children and adolescents. Paediatric Strategy Forums have been created to facilitate dialogue and provide an opportunity for constructive interactions between relevant stakeholders (patients/patient representatives, clinicians, academics, pharmaceutical companies and regulators) on topics requiring open discussion on development of medicines in the best interests of children and adolescents with cancer. The goal of this meeting is to share information, in a pre-competitive setting, to facilitate the developments of innovative medicines and ultimately their introduction into the standard-of-care of children with malignancies.

The first two Paediatric Strategy Forums were held at EMA in January and November 2017 on [ALK inhibition](#) and [mature B-cell malignancies](#), respectively. Both can be found in the [Paediatric medicines: Workshops](#) page in the European Medicines Agency website.

Immune checkpoint inhibitors have shown impressive success in some adult malignancies, in particular, monoclonal antibodies that block the interaction between programmed death ligand 1 (PD-L1) on the surface of tumor or antigen-presenting cells, and programmed death 1 (PD-1) on the surface of lymphocytes. Many of these products have now been licensed as first or second line treatments for adult malignancies. Furthermore, the combination of antibodies targeting PD-1 with those targeting the immune checkpoint molecule CTLA-4 has shown particularly high response rates especially in adult patients with metastatic melanoma. Early phase trials in children of single agent checkpoint inhibitors are currently being presented. High response rates are being observed in some cancers common to children and adults, for example in Hodgkin lymphoma. However, these results appear not to be reflected in typical paediatric malignancies. Some combination studies are in progress and others are planned. It therefore seems opportune to review the early results of these early phase trials in children and consider opportunities for paediatric studies in which check-point inhibitors are used in combination including also possible other approaches.

This Forum will review the immunological environment of paediatric malignancies, results from the use of checkpoint inhibitors in early phase clinical studies in paediatrics, strategies combining checkpoint inhibitors with other products and alternative immunotherapy strategies.

The output will be a published summary from all participants addressing the challenges and documenting the conclusions.

List of speakers and moderators

To be announced

Draft programme

5 September 2018

09:30: Registration

Please collect badges at the reception on the ground floor. The workshop will be held in room 03-F.

10.00: Welcome and introduction

Session 1

10.20: Immunological environment and immunotherapeutic challenge of paediatric malignancy

10.50: Review of Paediatric Investigation Plans of Checkpoint inhibitors

11.10: Results of Checkpoint inhibitors in early phase clinical studies

11.10 - 11.30 Pembrolizumab

11.30 - 11.50 Atezolizumab

11.50 - 12.10: Nivolumab

12.10 – 12.30: Ipilimumab

12.30: Lunch

Session 2

13.30: Development of checkpoint inhibitors in adults with lessons relevant to paediatrics

14.00: Checkpoint inhibitors

Biallelic mismatch repair, MSI status and tumour burden as potential predictive biomarkers and the way forward.

14.30: The way forward - Checkpoint inhibitors in lymphomas

- Non-Hodgkin's lymphoma
- Hodgkin's disease

15.30: Discussion - Monotherapy with checkpoint inhibitors in children

16.00: Coffee break

Session 3

16.30: The way forward - Checkpoint inhibitors in combination in other paediatric malignancies

16.30: Rationale design of clinical immunotherapy combination trials for maximum benefit and information

17.00: Checkpoint Inhibitors with chemotherapy/anti angiogenics:

- Pembrolizumab and chemotherapy - Hodgkin's
- Atezolizumab and standard of care
- Nivolumab and brentuximab bendamutisne, ipilimumab
- Avelumab and standard of care
- Avelumab and axitinib

18:30: Discussion: Combination with chemotherapy

19.30: Evening event

6 September 2018

Session 4

08.30: The way forward for checkpoint inhibitors in combination in other paediatric malignancies

08.30: Checkpoint Inhibitors with radiotherapy

- Minivan
- Cemiplimab and radiotherapy

Discussion: Combination with radiotherapy

09.45: Checkpoint Inhibitors with PARP Inhibitors

- Niraparib (Zejula)
- Tislelizumab

Discussion: Combination with PARP Inhibitors

10.00: Checkpoint Inhibitors with HDAC inhibitors

- Entinostat
- "INFORM2 NivEnt: a biomarker driven phase I/II combination study of Nivolumab and Entinostat

Discussion: Combination with HDAC inhibitors

10.30: Coffee

Session 4

11.00 Checkpoint Inhibitors with other checkpoint Inhibitors

CTLA-4

- Ipilimumab and nivolumab
- Tremelimumab and durvalumab

Anti-LAG-3

- Anti-LAG-3 mAb
- TSR-033

Discussion: Combination with other checkpoint Inhibitors

11.50 Combination of checkpoint Inhibitors with other immunoncology products

12.20 Combination of checkpoint Inhibitors with other immunoncology products

Monoclonal Antibodies:

- Bispecific CD20xCD3 antibody
- Isatuximab (CD38 monoclonal antibody)

Other:

- TSR 022 (anti -TIM-3)
- M7824 (bifunctional fusion protein combining a PD-L1 antibody and the extracellular domain of TGFβRII neutralizing TGFβ)

13.00 Lunch

Session 5

14.00 The way forward for checkpoint inhibitors in combination in other paediatric malignancies

14.00 – 14.50: Combination of checkpoint Inhibitors with other immunoncology products

- Oncolytic virus
- Anti TGF beta
- mRNA mixture
- mAb against CSF-1, MCS110

Discussion: Combination with other immunoncology products

14.50 - 15.20 Checkpoint Inhibitors with cell therapy

- Allogeneic cell therapy (ilixadencel, ATMP)
- ATIMP

Discussion: Combination with cell therapy

15.20: Strategic discussion and overall perspective

17.00: End of meeting
