Immune Checkpoint Inhibitors in the Early Setting: Past, Present & Future

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January 2024

Disclosures

Advisory role: Amgen, AstraZeneca, Bayer, Daiichi, EISAI, Genomic Health, Hengrui, Innate, Ipsen, Leo Pharma, Lilly, Merck, MSD, Novartis, Pfizer, Seattle Genetics, Menarini

Speaker fees: Amgen, AstraZeneca, Bayer, Daiichi, EISAI, Genomic Health, Ipsen, Leo Pharma, Lilly, Merck, MSD, Novartis, Pfizer, Seattle Genetics

Research grants to my Institute: BMS, Roche

Achievements of ICI in the advanced setting (1)

Primary tumor	Outcome benefit	
	YES	NO
CNS[1]		✓
H&N (Sq[2] + NPC[3])	✓	
Upper GI[4,5]	✓	
Hepatic[6] & biliary[7]	✓	
CRC (MSI high)[8]	✓	
CRC (MSI low)[8]		✓
Pancreatic[9]		✓

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CNS, central nervous system; GI, gastrointestinal; H&N, head and neck; ICI, immune checkpoint inhibitor; MSI, microsatellite instability; NPC, nasopharyngeal cancer; Sq, squamous.

Achievements of ICI in the advanced setting (2)

Primary tumor	Outcome benefit	
	YES	NO
RCC[1]	✓	
Bladder[2]	✓	
Prostate[3]		✓
Ovarian[4,5]		✓
Endometrial[6]	✓	
Cervical[7]	✓	

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ICI, immune checkpoint inhibitor; RCC, renal cell carcinoma.

Achievements of ICI in the advanced setting (3)

Primary tumor	Outcome benefit	
	YES	NO
Melanoma[1]	✓	
Cutaneous (Merkel;[2] Sq[3])	✓	
Sarcoma[4,5]		✓
NSCLC[6]	✓	
SCLC[7]	✓	
TNBC[8]	✓	
Luminal BC[8]		✓
HER-2 positive BC[8]		✓

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BC, breast cancer; HER-2, human epidermal growth factor receptor 2; ICI, immune checkpoint inhibitor; NSCLC, non-small cell lung cancer; SCLC, small-cell lung cancer; Sq, squamous; TNBC, triple negative breast cancer.

ICI-based combinations in the early setting

- ICI alone
- ICI + ICI (e.g., CTLA-4; LAG-3)
- ICI + Chemotherapy (or ADC)
- ICI + Chemotherapy + RT concomitantly (H&N; cervix)
- ICI + molecular-targeted therapies (e.g., VEGFR inhibitors,…)

ADC, antigen dependent cytotoxicity; CTLA-4, Cytotoxic T-lymphocyte associated protein 4; H&N, head and neck; ICI, immune checkpoint inhibitor; LAG-3, Lymphocyte-Activation Gene 3; RT, radiotherapy; VEGFR, vascular endothelial growth factor receptor.

Achievements of ICI in the early setting of solid tumors

Primary tumor	Outcome benefit		
	Neoadjuvant	Adjuvant	Comments
Esophagus[1]		✓	Organ sparing?!
CRC (MSI high)[2]	✓		Organ sparing?!
RCC[3]		✓	Only 1 of 4 trials positive
Bladder[4]	✓	✓	Organ sparing?!
Melanoma[5]	✓	✓	Great benefit in high risk pts
Merkel[6]	✓		Less mutilated surgery
NSCLC[7]	✓	✓	Great benefit
TNBC[8]	✓	✓	Great benefit
Luminal BC[8]	✓		Promising early results in need for consolidation

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BC, breast cancer; CRC, colorectal carcinoma; ICI, immune checkpoint inhibitor; RCC, renal cell carcinoma; TNBC, triple negative breast cancer.

Achievements of ICI in the early setting of solid tumors: open questions (1)

- Neoadjuvant versus adjuvant vs both?
- ICI alone or in combination?
- Neoadjuvant ICI: is there any correlation between pCR rate and outcome?
- Role of adjuvant ICI in pts with pCR post ICI-based neoadjuvant therapy?
- Role of ICI in residual disease based on circulating tDNA?
- Role of priming with ICI before induction therapy?

ICI, immune checkpoint inhibitor; pCR, pathological complete response; tDNA, tumour DNA.

Achievements of ICI in the early setting of solid tumors: open questions (2)

- Role of induction ICI-based before concomitant CT/RT in selected tumors (e.g., Nasopharyngeal Cancer)?
- Role of radiation/other approaches in ICI-based combination to transform « cold » tumors into « hot » tumors (e.g., Luminal BC)?
- Why there was a discrepancy in benefit outcome in the same tumor/setting by using different ICI (e.g., adjuvant ICI in ccRCC)?

BC, breast cancer; ccRCC, clear cell renal cell carcinoma; CT, chemotherapy; ICI, immune checkpoint inhibitor; RT, radiotherapy.

Achievements of ICI in the early setting of solid tumors: open questions (3)

- Role of ICI in combination with new therapeutic approaches (bispecific, ADCs, vaccines,…)
- Role of ICI in pre-cancerous lesions (e.g., leukoplakia,..) and *in situ* tumors (e.g., superficial bladder cancer,…)
- Duration of ICI therapy (pre- and post- local therapy)?
- Optimal doses and schedules of ICI?

ADC, antigen dependent cytotoxicity; ICI, immune checkpoint inhibitor.

Conclusions and perspectives (1)

1. ICI are a therapeutic backbone in several advanced solid tumors that demonstrate significant clinical benefit
2. ICI are a therapeutic backbone in some solid tumors in the early setting
3. Accumulating data consolidate the value of ICI in Loco tumor (+ regional lymph nodes) with regards to efficacy in the neoadjuvant setting

ICI, immune checkpoint inhibitor.

Conclusions and perspectives (2)

4. **Currently, with the available data, no common statements for all solid tumors/ICI types in relation to treatment benefit in the early setting. Randomized clinical trials results remain key to conclude**

ICI, immune checkpoint inhibitor.

Conclusions and perspectives (3)

5. **There remains many open questions needing answers through well-designed clinical trials (!Academic trials)**

6. **Beyond PD-1/PD-L1/CTLA4 inhibitors, we are moving to new generations of immune therapy approaches (value in early setting is under investigation?)**

CTLA-4, Cytotoxic T-lymphocyte associated protein 4; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1.

Thank you

Enjoy your first workshop!

	PLENARY	WORKSHOPS		
	SATIN ROOM FLOOR 3	METEOR ROOM FLOOR 1	COMET ROOM FLOOR 2	SATIN ROOM FLOOR 3
16.30	16.30 INTRODUCTION P LACANTE & P COULIE			
16.40	16.40 PLENARY 1 Moving cancer Immunotherapy towards earlier stages of disease P.COULIE A. AWADA			
17.25		17.25=>18.05 Imaging for Immunotherapy management V VANDECAVEYE F COUSIN G JERUSALEM (Mod)	17.25=>18.05 When to stop or resume immunotherapy? B NEYNS J VANSTEENKISTE E VAN CUTSEM (Mod)	17.25=>18.05 What's new in traeting Immunotherapy toxicity? S RAUH S ASPESLAGH
18.05-18.20	BREAK			

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