Consulting, lecturing or advisory role
Astellas, Astra Zeneca, BMS, Celgene, Five Prime Therapeutics, Gritstone Oncology, Merck, Servier
EDUCATIONAL GOALS

- Immunogenicity of microsatellite high (MSI-H) and microsatellite stable (MSS) colorectal cancer
- Role of immune checkpoint blockade in MSI-H mCRC
- Reasons for lack of efficacy of immunotherapy in MSS mCRC
- Efforts to overcome immune evasion in MSS mCRC
- Overview early results of immunotherapy in anal SCC
I. COLORECTAL CANCER
In CRC high mutation burden is often related to IO efficacy

Immune checkpoint blockade efficacy

POLE mut

MSI-H

Low mutation burden
COLORECTAL CANCER AND IMMUNOTHERAPY

MMRd vs MMRp tumours

From an immunotherapy perspective there are two CRC categories

1. **Mismatch repair deficient (MMRd)** – 2-5% of Stage IV cancers, more common in Stage II>III
2. **Mismatch repair proficient (MMRp)** - majority of Stage IV cancers

Mismatch repair status can be assessed using:

- **Protein immunohistochemistry for MMR proteins** (MLH1, MSH2, MSH6 and PMS2)
- **PCR** to detect high levels of microsatellites in DNA (microsatellite instablility, **MSI**)
- Next generation sequencing

>80% of MMRd tumours are sporadic (methylation of MLH1), however as 15-20% may be germline (Lynch syndrome) genetics referral should be considered in MMRd patients (pending algorithm BRAF/MLH1 methylation studies for MLH1 deficient patients).
MISMATCH REPAIR DEFICIENCY AND THE IMMUNE SYSTEM

1. Insertion mutation in coding microsatellites leading to frameshift mutation

2. Translation of frameshift peptides

3. Processing and presentation of frameshift peptides

ER

Neoantigen-MHC class I

CD8+ T cells

Anti-PD-L1 Antibody

PD-L1

Anti-PD-1 Antibody

PD-1

Baretti et al, Pharmacol Ther. 2018
PEMBROLIZUMAB IN MMRD AND MMRP CRC

- MMRP or MMRD (loss of MLH1, MSH2, MSH6 or PMS2, or MSI in ≥ 2 loci)
- ≥ 2 prior cancer therapy regimens

<table>
<thead>
<tr>
<th>Outcome</th>
<th>MMRD CRC (n = 28)</th>
<th>MMRP CRC (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR, %</td>
<td>57</td>
<td>0</td>
</tr>
<tr>
<td>Response, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>PR</td>
<td>46</td>
<td>0</td>
</tr>
<tr>
<td>SD</td>
<td>32</td>
<td>16</td>
</tr>
<tr>
<td>PD</td>
<td>4</td>
<td>44</td>
</tr>
<tr>
<td>NE</td>
<td>7</td>
<td>40</td>
</tr>
<tr>
<td>Median PFS, mos</td>
<td>NR</td>
<td>2.3</td>
</tr>
<tr>
<td>Median OS, mos</td>
<td>NR</td>
<td>6.0</td>
</tr>
</tbody>
</table>

May 2017 – FDA licensed pembrolizumab in previously treated MMRD colorectal cancer

Le DT, et al. ASCO 2016. Abstract 103
Le DT et al, NEJM 2015

Le DT et al. ASCO 2016. Abstract 103
Le DT et al, NEJM 2015
Responses observed in all lines of therapy
Benefits of anti-PD-1 therapy are sustained in MMRd CRC
76% alive at one year follow up
NIVOLUMAB FOR MMRD-CRC
CHECKMATE-142

- Histologically confirmed metastatic or recurrent CRC
- dMMR/MSI-H per local laboratory
- ≥ 1 prior line of therapy

Primary endpoint:
- ORR per investigator assessment

Other key endpoints:
- ORR per BICR, DCR, DOR, PFS, OS, and safety
NIVOLUMAB FOR MMRD-CRC
CHECKMATE-142

- 60% of patients had a reduction in tumor burden from baseline with nivolumab monotherapy

### Benefits of nivolumab in MMRD CRC very similar to those observed for pembrolizumab

**ORR 34%**

<table>
<thead>
<tr>
<th>Best overall response, n (%)</th>
<th>All patients¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR, n (%)</td>
<td>25 (34)</td>
</tr>
<tr>
<td>[95% CI]</td>
<td>[23.2, 45.7]</td>
</tr>
<tr>
<td>CR</td>
<td>7 (9)</td>
</tr>
<tr>
<td>PR</td>
<td>18 (24)</td>
</tr>
<tr>
<td>SD</td>
<td>23 (31)</td>
</tr>
<tr>
<td>PD</td>
<td>22 (30)</td>
</tr>
<tr>
<td>Unable to determine</td>
<td>4 (5)</td>
</tr>
</tbody>
</table>

**Disease control, n (%)²**

| [95% CI] | 46 (62) |

Overman, Lancet Oncol 2017
Anti-PD1 therapy is a good choice for MMRd patients regardless of family history, BRAF status or PD-L1 expression.
NIVOLUMAB FOR MMRD-CRC
CHECKMATE-142

Median PFS 6.6 months
Median PFS 4.2m (A) vs NR(B)

Median OS not reached
12 month OS 68% (A) vs 81%(B)

48% progression free and 74% alive at 1 year

August 2017 – FDA licensed nivolumab in MMRD colon cancers
NIVOLUMAB FOR MMRD-CRC
CHECKMATE-142

No responding patient relapsed during follow up
COMBINATIONS
NIVOLUMAB + IPILIMUMAB for MMRd-CRC : CHECKMATE-142

Phase 2 Nonrandomized Study

- Histologically confirmed metastatic or recurrent CRC
- dMMR/MSI-H per local laboratory
- ≥ 1 prior line of therapy

Combination cohort

Nivolumab 3 mg/kg + ipilimumab 1 mg/kg Q3W
(4 doses and then nivolumab 3 mg/kg Q2W)

Monotherapy cohort

Nivolumab 3 mg/kg Q2W

Primary endpoint:
- ORR per investigator assessment (RECIST v1.1)

Other key endpoints:
- ORR per BICR, DCR, a
- DOR, PFS, OS, and safety

Overman et al, JCO 2018
NIVOLUMAB + IPILIMUMAB FOR MSI-CRC

Investigator assessed response

ORR to combination therapy appears greater than nivolumab alone (no formal comparison planned)

Andre et al, ASCO GI 2018
Overman et al, Journal of Clinical Oncology 2018
NIVOLUMAB + IPILIMUMAB FOR MSI-CRC
Progression free and overall survival

<table>
<thead>
<tr>
<th></th>
<th>Nivolumab + ipilimumab(^{a,b})</th>
<th>Nivolumab + ipilimumab(^{a,d})</th>
</tr>
</thead>
<tbody>
<tr>
<td>9-month rate (95% CI), %</td>
<td>76 (67.0, 82.7)</td>
<td>87 (80.0, 92.2)</td>
</tr>
<tr>
<td>12-month rate (95% CI), %</td>
<td>71 (61.4, 78.7)</td>
<td>85 (77.0, 90.2)</td>
</tr>
</tbody>
</table>

Combination nivolumab/ipilimumab results in 71% 12 month progression free survival and 85% one year overall survival
# NIVOLUMAB + IPILIMUNAB FOR MSI-CRC
## Safety data

<table>
<thead>
<tr>
<th>Patients, n (%)</th>
<th>Nivolumab + ipilimumab N = 119</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any grade</td>
</tr>
<tr>
<td>Any TRAE</td>
<td>87 (73)</td>
</tr>
<tr>
<td>Any serious TRAE</td>
<td>27 (23)</td>
</tr>
<tr>
<td>Any TRAE leading to discontinuation</td>
<td>15 (13)°</td>
</tr>
</tbody>
</table>

**TRAEs reported in > 10% of patients**

- Diarrhea: 26 (22) / 2 (2)
- Fatigue: 21 (18) / 2 (2)
- Pruritus: 20 (17) / 2 (2)
- Pyrexia: 18 (15) / 0
- Increased AST: 17 (14) / 9 (8)
- Hypothyroidism: 16 (13) / 1 (1)
- Nausea: 15 (13) / 1 (1)
- Increased ALT: 14 (12) / 8 (7)
- Rash: 13 (11) / 2 (2)
- Hyperthyroidism: 13 (11) / 0

**Toxicity with combination ipilimumab plus nivolumab**

- 10% patients discontinued treatment
MOVING IMMUNOTHERAPY INTO EARLIER LINES
CHECKMATE 142 1L cohort

• Histologically confirmed metastatic or recurrent CRC
• MSI-H/dMMR per local laboratory

Previously treated

NIVO3 Q2W

NIVO3 + IPI1 Q3W
(4 doses and then NIVO3 Q2W)

Previously treated

1L

NIVO3 Q2W + IPI1 Q6W

Primary endpoint:
• ORR per investigator assessment (RECIST v1.1)

Other key endpoints:
• ORR per BICR, DCR, DOR, PFS, OS, and safety

Lenz et al, ESMO 2018
NIVOLUMAB AND IPILIMUMAB IN 1L
CHECKMATE 142 1L cohort

ORR 60%

ORR not compromised by low dose ipilimumab

Lenz et al, ESMO 2018
NIVOLUMAB AND IPILIMUMAB IN 1L
CHECKMATE 142 1L cohort

<table>
<thead>
<tr>
<th>PFS*</th>
<th>NIVO3 (Q2W) + IP11 (Q6W)</th>
<th>N = 45</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median PFS, months (95% CI)</td>
<td>NR (14.1–NE)</td>
<td></td>
</tr>
<tr>
<td>9-mo rate (95% CI), %</td>
<td>77 (62.0–87.2)</td>
<td></td>
</tr>
<tr>
<td>12-mo rate (95% CI), %</td>
<td>77 (62.0–87.2)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>OS*</th>
<th>NIVO3 (Q2W) + IP11 (Q6W)</th>
<th>N = 45</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median OS, months (95% CI)</td>
<td>NR (NE)</td>
<td></td>
</tr>
<tr>
<td>9-mo rate (95% CI), %</td>
<td>89 (74.9–95.1)</td>
<td></td>
</tr>
<tr>
<td>12-mo rate (95% CI), %</td>
<td>83 (57.6–91.7)</td>
<td></td>
</tr>
</tbody>
</table>
Nivolumab plus low dose ipilimumab is a safe and effective choice for MMRd CRC (not yet licensed)

<table>
<thead>
<tr>
<th></th>
<th>Nivo + q3wk ipi</th>
<th>Nivo + q6wk ipi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 3-4 TRAE</td>
<td>32%</td>
<td>16%</td>
</tr>
<tr>
<td>Serious TRAE</td>
<td>20%</td>
<td>7%</td>
</tr>
<tr>
<td>Discontinuation</td>
<td>10%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Lenz et al, ESMO 2018
NEOADJUVANT IMMUNOTHERAPY FOR MMRD CRC

Neoadjuvant nivolumab plus ipilimumab: NICHE study

*MMR protein staining for MLH1, PMS2, MSH2, MSH6
NEOADJUVANT IMMUNOTHERAPY FOR MMRD CRC

Neoadjuvant nivolumab plus ipilimumab

No residual tumour in MMRD patients treated with nivolumab plus ipilimumab

Chalabi et al, ESMO 2018
# Neoadjuvant Immunotherapy for MMRD CRC

Neoadjuvant nivolumab plus ipilimumab

<table>
<thead>
<tr>
<th></th>
<th>dMMR (n=7)</th>
<th>pMMR (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age-yr (range)</td>
<td>60.9 (41 - 75)</td>
<td>63.1 (44 - 73)</td>
</tr>
<tr>
<td>Female sex – no. (%)</td>
<td>4 (57%)</td>
<td>5 (62%)</td>
</tr>
<tr>
<td>CEA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>≥5</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Clinical disease stage – no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I/II</td>
<td>3 (43%)</td>
<td>5 (62%)</td>
</tr>
<tr>
<td>III</td>
<td>4 (57%)</td>
<td></td>
</tr>
<tr>
<td>Tumor location</td>
<td></td>
<td></td>
</tr>
<tr>
<td>left</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>right</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Lynch syndrome – no. (%)</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>TMB* – median (range)</td>
<td>1795 (1324 - 4458)</td>
<td>103 (68 – 269)</td>
</tr>
</tbody>
</table>

No/minimal effect of MMRp patients treated with nivolumab plus ipilimumab
BIOMARKERS IN MMRD CRC
Does tumour mutation burden matter?

High TMB was associated with higher change of radiological response, and improved PFS and OS
Caveat – small dataset (n=22), targeted panel to assess TMB
BIOMARKERS IN MMRD CRC

Markers of resistance and secondary targets

- Recurrent mutations and LOH in antigen presenting machinery (HLA, B2M) in MSI tumours
- JAK1/2 mutations

- High incidence of TRK, ALK, ROS fusions – consider referring for screening for clinical trials
- Synthetic lethality with Werner helicase inhibition

Grasso et al, Cancer Discovery 2018
Shin et al, Cancer Discover 2016
Pietrantonio et al, JCNI 2017
Bass, Nature 2109
Conclusions

- Anti-PD-1 is a standard of care for MMRD CRC associated with high response rates and durable benefit
- European license awaited
- Dual immunotherapy blockade is another standard, low dose ipilimumab appears safe and tolerable
- Moving immune checkpoint blockade to earlier lines of therapy is an exciting prospect
IMMUNOTHERAPY FOR MMRP CRC
## CHECKPOINT IMMUNE BLOCKADE IS INEFFECTIVE IN MSS CRC

<table>
<thead>
<tr>
<th>Author</th>
<th>Disease</th>
<th>Drug</th>
<th>N</th>
<th>ORR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Le et al</td>
<td>MSS CRC</td>
<td>Pembrolizumab</td>
<td>18</td>
<td>0%</td>
</tr>
<tr>
<td>Overman et al</td>
<td>MSS CRC</td>
<td>Nivolumab + ipilimumab</td>
<td>20</td>
<td>5%</td>
</tr>
<tr>
<td>Chung et al</td>
<td>Refractory CRC</td>
<td>Tremelimumab</td>
<td>49</td>
<td>2%</td>
</tr>
<tr>
<td>Topialan et al</td>
<td>Refractory CRC</td>
<td>Nivolumab</td>
<td>19</td>
<td>0%</td>
</tr>
</tbody>
</table>

COLORECTAL CANCER MOLECULAR AND IMMUNE LANDSCAPE

Gunney et al, Nat Med. 2015 Nov;21(11):1350-6
Most current WNT inhibitors are upstream of APC mutation. High beta-catenin expression results in low CD3 and CD8 infiltrate. Targeting WNT is challenging. Most inhibitors are upstream of APC; exception porcupine inhibitors.
In preclinical models, inhibition of MEK signalling leads to ↑ CD8 T cell infiltration and MHC1 expression. Combination of MEKi and anti-PD-L1 showed synergy.
Early results were positive

<table>
<thead>
<tr>
<th>BOR (n = 84)a</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>7 (8%)</td>
</tr>
<tr>
<td>CR</td>
<td>0</td>
</tr>
<tr>
<td>PR</td>
<td>7 (8%)</td>
</tr>
<tr>
<td>SD</td>
<td>19 (23%)</td>
</tr>
<tr>
<td>DCR</td>
<td>26 (31%)</td>
</tr>
<tr>
<td>PD</td>
<td>51 (61%)</td>
</tr>
</tbody>
</table>

Best response: Partial response, Stable disease, Progressive disease

MSI status: S MSS, L MSI-low, H MSI-high

Bendell et al, ASCO GI 2018
TARGETING MAPK AND IMMUNE IN CRC

Cobemetanib plus atezolizumab in mCRC: IMBLAZE

ORR <3% in all arms
No difference in PFS or OS
Outcome not different in RAS mt patients

Future questions
Scheduling of MEKi – effect on T-cells
MEK signatures
Novel IO combinations
RAS mutant only trials

Bendell et al, Lancet Oncol 2019
Role for CXCR3

- KRAS mutation decreases IRF2 expression
- Decreased IRF2 leads to increased CXCL3 expression
- CXCL3 acts on CXCR2 on MDSC to attract to TME
- MDSC causes immunosuppression

- In mouse models, inhibition of CXCR2 leads to increased sensitivity to immunotherapy

Liao et al, Cancer Cell 2019
TARGETING TGF-B IN CMS 4 CRC

**CMS4 Mesenchymal**

- 23%
- SCNA high
- Stromal infiltration, TGFβ activation, angiogenesis
- Worse relapse-free and overall survival

**M7824**

- Bifunctional fusion protein targeting PD-L1 and TGF-β

1 CRC responder:

**MSS, CMS4, KRAS mutant** and PD-L1+, high signature for complement cascade and **MDSC**

Ongoing clinical trial in CMS4 CRC

Lan et al, Sci Trans Med 2018

Kopetz et al, ASCO GI 2018
**WHAT ELSE CAN WE DO TO TURN COLD CRC HOT?**

<table>
<thead>
<tr>
<th>Combination IO strategy</th>
<th>Radiotherapy</th>
<th>Anti-angiogenics + IO</th>
<th>Bispecifics</th>
<th>Increase innate immunity</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Anti-CTLA4+PD-L1</td>
<td>• RT + Anti-CTLA4+PD-L1</td>
<td>• Bevacizumab + atezolizumab</td>
<td>• CEA-TCB</td>
<td>• MGN 1703</td>
</tr>
<tr>
<td>• Anti-NKG2A + PD-L1</td>
<td></td>
<td>• Regorafenib + nivolumab</td>
<td>• CEA-TCG+atezolizumab</td>
<td></td>
</tr>
<tr>
<td>• Anti-TGFb+anti-PD-L1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
COMBINATION IO: ANTI-CTLA-4 + ANTI-PD-L1

**Concerns**

1. Extra interventions in experimental arm
2. High alpha 0.1 risks false positive
3. No PFS correlate for OS benefit
4. No responses in experimental arm
Using a cut off of TMB of ≥28 in ctDNA discriminated two groups with differential benefit from combination treatment.

Caveat: high TMB group is larger than other datasets, requires further validation.

Chen et al, ASCO GI 2019
RADIOTHERAPY DOSE AND IMMUNE RESPONSE

Vanpouille-Box et al, Nature Comm 2017,
Caveat:
Small dataset with no control
33% did not reach RT due to toxicity, PD or withdrawal

Hubbard et al, ASCO 2019
ANTI-ANGIOGENESIS
MODUL: MAINTENANCE CAPECITABINE/BEVACIZUMAB +/- ATEZOLIZUMAB

Grothey et al, ESMO 2018
BACCI: CAPECITABINE/BEVACIZUMAB +/- ATEZOLIZUMAB

Primary Endpoint: PFS
Secondary Endpoints: OS, RR, safety

Metastatic colorectal cancer
- Progression on 5-FU or Cape, oxaliplatin, irinotecan, bevacizumab, anti-EGFR antibody (RAS wt)
- ECOG 0-1
- Life expectancy > 3 mo
- No prior PD-L1/PD-1 therapy

Randomization: 2:1

Capecitabine/bevacizumab + atezolizumab (n=87)
- Capecitabine 850 or 1000 mg/m2 qd 1-21
- Bevacizumab 7.5 mg/kg IV qd
- Atezolizumab 1240 mg IV qd
- Cycle Length = 21 dd

Capecitabine/bevacizumab + placebo (n=46)

Characteristic | Cape/Bev + Placebo (n=46) | Cape/Bev + Atezo (n=82) | Total (n=128)
--- | --- | --- | ---
Mean Age (yrs) | 56.5 | 59.6 | 58.5
Male Gender | 30 (65.2%) | 47 (57.3%) | 77 (60.2%)
White Race | 36 (78.3%) | 66 (80.5%) | 102 (79.7%)
ECOG 0 | 21 (45.7%) | 39 (47.6%) | 60 (46.9%)
Colon | 27 (56.7%) | 57 (69.5%) | 84 (65.6%)
Rectum | 19 (41.3%) | 25 (30.5%) | 44 (34.4%)
RAS mutant | 25 (54.3%) | 49 (59.8%) | 74 (57.8%)
RAS wildtype | 21 (45.7%) | 33 (40.2%) | 54 (42.2%)
MSI Missing | 1 | 5 | 6
MSI/pMMR | 39 (86.7%) | 66 (85.7%) | 105 (82.1%)
MSI-HidMMR | 6 (13.3%) | 11 (14.3%) | 17 (13.9%)

PROGRESSION FREE SURVIVAL

ORR 2/46
4.35% (0.53-14.8)

ORR 7/82
8.54% (3.5-16.8)

OVERALL SURVIVAL

Logrank P-value (1-sided) = 0.051

Logrank P-value (1-sided) = 0.388
NIVOLUMAB AND REGORAFENIB

Figure 1. Duration of Treatment

Median duration of treatment was 6.1 months (range 0.7-14.9 months) Study treatment is ongoing in 21 patients.
BRINGING THE T CELLS TO THE TUMOUR: CEA BISPECIFIC

Study 1: CEA-TCB monotherapy
n = 31, 60-600 mg

Best change in target lesions from baseline, %

ORR 6%

Study 2: CEA-TCB + atezolizumab
n = 25, 5-160 mg

Best change in target lesions from baseline, %

ORR 18%
INCREASING INNATE IMMUNITY
IMPALA MAINTENANCE TRIAL

Lefitolimod (MGN 1703)
TLR9 agonist
Activates innate immune system NK, monocytes, release IP-10 cytokine
Increases uptake tumour associated antigens

Salazar et al, ESMO 2019
Lefitolimod (MGN 1703) TLR9 agonist
Activates innate immune system NK, monocytes, release IP-10 cytokine
Increases uptake tumour associated antigens

Salazar et al, ESMO 2019
WHAT WORKS TO TURN COLD CRC HOT?

CMS2
Target WNT

CMS3
MEKi + IO

CMS4
TGFB + IO

Combination IO strategy
Anti-CTLA4+PD-L1

Radiotherapy
RT + Anti-CTLA4+PD-L1
Anti-angiogenics + IO
Bevacizumab + atezolizumab

Bispecifics
CEA-TCB
CEA-TCB + atezolizumab

Increase innate immunity
MGN 1703

Possibly TMB high

(Very) early data

The search continues….
II. ANAL CANCER
RATIONALE FOR IMMUNOTHERAPY IN ANAL CANCER

90% HPV positive
NIVOLUMAB IN ANAL CANCER
First evidence of efficacy of anti-PD1 in anal cancer

PD-L1 unselected
ORR 24%

Median PFS 4.1 months
Median OS 11·5 months

Increased ORR in high CD8 and PDL1
Small numbers”
All patients were PD-L1 positive (74% of screened)
  Mostly pretreated
  ORR 17% (4/24 SCC patients)

Median PFS 3.5 months (95% CI 1.7–7.3 months)
Median OS 9.3 months (95% CI, 5.9 months to not reached)
ANAL CANCER BIOMARKERS

HPV ctDNA as a prognostic and response metric

HPV ctDNA after chemotherapy is prognostic

HPV ctDNA under anti-PD-1 therapy

Bernard-Tessier et al, CCR 2019
Cabel et al, IJC 2017
ANAL CANCER AND IMMUNOTHERAPY

Summary

- Anal carcinoma is a virally driven, immunogenic tumour
- Preliminary results in previously treated patients are encouraging
- Randomised data and integration into earlier lines of therapy are awaited
THANK YOU

Dr Elizabeth Smyth
Cambridge University Hospitals NHS Foundation Trust