WHICH IMMUNOTHERAPY IS THE STANDARD IN 1ST LINE MRCC TREATMENT:

IMMUNE DOUBLET

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DISCLOSURE OF INTEREST

**Employment:** University Hospital Essen

**Honoraria for speaker engagements and advisory roles:** Art tempi, AstraZeneca, Astellas, BMS, Cerulean, COCS, ClinSol, EUSAPharm, EISAI, Ipsen, MedUpdate, Merck Serono, MSD Merck, MedKomAkademie, Novartis, NewConceptOncology, Lilly, Johnson & Johnson, PharmaMar, PeerVoice, Pfizer, Roche, StreamedUp!, ThinkWired!

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**Ownership of any stocks and shares:** AstraZeneca, BMS, MSD
TKI - GREAT FOR PALLIATION, BUT WHERE ARE THE CRS?

TKI are devote of significant complete responses

IPILIMUMAB WITH LONGEST FOLLOW-UP AND BEST CR RATES

Similar ORR in all risk-groups

**DURATION OF RESPONSE IS OF IMPORTANCE**

CM214 has longest FU and compelling outcome

**CM214**

Median duration of response per investigator:
- Nivolumab plus ipilimumab NR (95% CI 24.7–NE) vs sunitinib 18.0 months (13.8–22.2)
- HR 0.51 (95% CI 0.38–0.68)

**KN426**


EPAR Pembrolizumab: EMA/CHMP/455620/2019 25.07.19
# IPILIMUMAB + NIVOLUMUMAB ACHIEVED HIGHEST CR RATE

<table>
<thead>
<tr>
<th>Study</th>
<th>Atezolizumab</th>
<th>Nivolumab*</th>
<th>Pembrolizumab</th>
<th>Pembrolizumab + axitinib</th>
<th>Avelumab + axitinib</th>
<th>Atezolizumab + Bevacizumab*</th>
<th>Ipilimumab + nivolumab</th>
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<td>IM150</td>
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| ORR, %    | 25 | 28.7 | 36.4 | 59.3 | 51.4 | 37.0 | 41.3 |
| CR, %     | 11 | 1.9  | 2.7  | 5.8  | 3.4  | 5.0  | 10.5 |
| PR, %     | 14 | 26.9 | 33.6 | 53.5 | 48.0 | 31.0 | 30.7 |
| SD, %     | -  | 24.1 | 31.8 | 24.5 | 29.6 | 39.0 | 30.0 |
| PD, %     | -  | 32.4 | 30.0 | 10.9 | 11.5 | 18.0 | 22.0 |
| NE, %     | -  | 14.8 | 1.8  | 3.5  | 5.7  | 7.0  | 6.7  |

Different follow-up is reported between trials


*without license
A LARGER FRACTION DERIVES BENEFIT FROM IPI-NIVO

42% have tumor shrinkage >50%

Grünwald ESMO 2019: 950P
IPILIMUMAB + NIVOLUMAB HAS BETTER TOLERABILITY

Less grade $\geq 3$ AEs and better HR-QoL than sunitinib

Grade 3-4 TRAE:

- Nivolumab group: 46.6%
- Sunitinib group: 63.9%


FAVORABLE TOLERABILITY FOR IPI-NIVO

VEGF INHIBITION IS ASSOCIATED WITH DECREASE IN QOL
Drop in HR-QoL even with bevacizumab + atezolizumab

SE, standardized error. Score range, 0-76. Effect size ≥ 0.20 suggests a clinically important difference between arms.

Mean baseline total scores (SD): atezo + bev, 59.8 (9.8) vs sunitinib, 59.5 (9.4). Mean normative FKSI-19 total score for the US general adult population, 59.8.

* P < 0.05 from repeated-measures model for atezo + bev vs sunitinib at visits until week 72; exception was at week 6.

** Average difference in least-squares mean estimates of score changes for atezo + bev vs sunitinib at visits through week 54 was 3.67; mean effect size, 0.42 (range, 0.16, 0.67).

P < 0.0001 from linear mixed model of change from baseline to end of treatment; effect size, 0.35. 1. Butt et al. Cancer. 2013;119:429-437.
KN426: WITHOUT HR-QOL-BENEFIT FOR AXITINIB + PEMBROLIZUMAB

**EORTC QLQC30**

**Time to Deterioration (FKSI-DRS)**

HR 1.44 (95% CI 1.14-1.82)

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CONCLUSIONS

• IPI-NIVO achieved the highest fraction of CRs
• Durability of CPI-induced responses is better than with TKI
• Quality of response is a key component for improved clinical outcome
• There are no signs of detrimental tolerability for IPI-NIVO
• HR-QoL improved during treatment with IPI-NIVO and is better than with sunitinib
• AXI-PEMBRO has no improvement in HR-QoL (in fact: time to deterioration is better with sunitinib)
• AXI-PEMBRO or AVELU have short FU and longevity of outcome data cannot be assessed, yet
• Overall, IPI-NIVO exerts many benefits and should be the preferred 1st line choice