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MEETING SUMMARY
ASCO 2020, VIRTUAL MEETING

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HIGHLIGHTS FROM GU NURSES CONNECT
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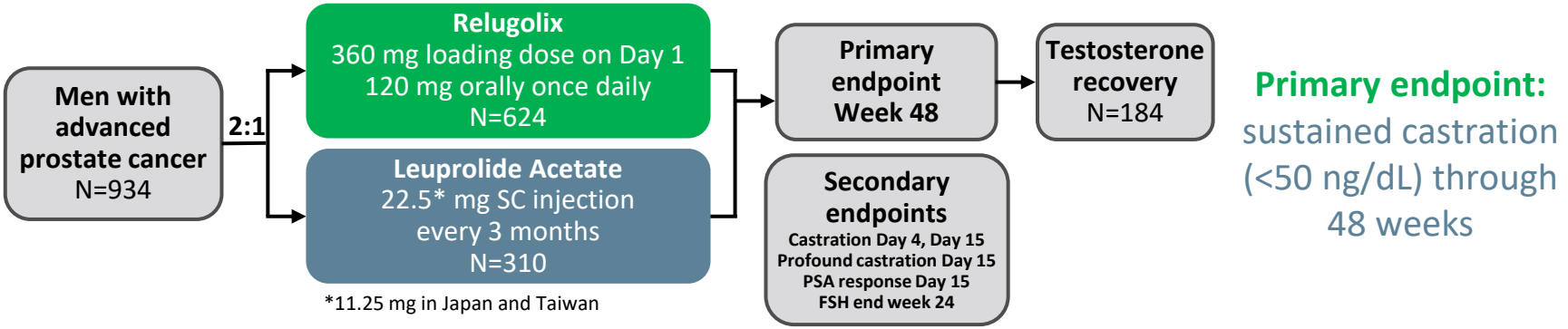
HERO PHASE 3 TRIAL: RESULTS COMPARING RELUGOLIX, AN ORAL GnRH RECEPTOR ANTAGONIST, VERSUS LEUPROLIDE ACETATE FOR ADVANCED PROSTATE CANCER

Shore N, et al.
ASCO 2020. Abstract #5602. Oral presentation

HERO STUDY: BACKGROUND

- Androgen deprivation therapy **(ADT)** is the **mainstay of treatment for advanced or metastatic prostate cancer**[1]
- Gonadotropin-releasing hormone **(GnRH) agonists**, such as leuprolide acetate, **are the most commonly used ADT for medical castration**. However **they cause an initial testosterone surge** with a delayed onset of castration and require depot injection[2]
- **Relugolix is an oral, GnRH receptor antagonist** in development for the treatment of men with advanced prostate cancer[3,4]
- **HERO, a global, pivotal, phase 3 trial**



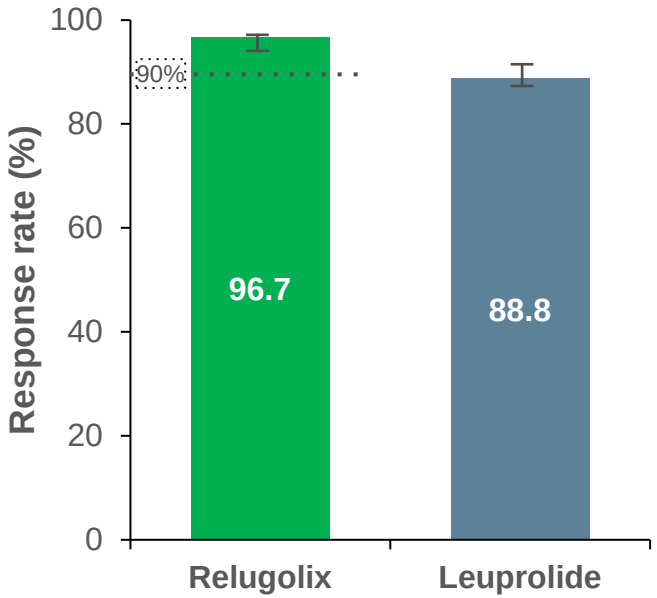
Primary endpoint: sustained castration (<50 ng/dL) through 48 weeks

ADT, androgen deprivation therapy; FSH, follicle stimulating hormone; GnRH, gonadotropin-releasing hormone; PSA, prostate specific antigen; SC subcutaneous

1. Schröder F, et al. BJU Int 2012; 109(Suppl 6):1-12; 2. Shore N, et al. Prostatic Dis 2013; 16: 7-15; 3. Shore N, et al. ASCO 2020. Abstract #5602. Oral Presentation; 4. Shore N, et al. N Engl J Med 2020. DOI: 10.1056/NEJMoa2004325

HERO STUDY: RESULTS

PRIMARY ENDPOINT



. . . **Primary endpoint success criterion:**
Relugolix lower boundary of 95% CI ≥90%

Difference between treatments demonstrated non-inferiority and superiority of relugolix to leuprolide [7.9 %; 95% CI: 4.1-11.8%, p<0.001]

SECONDARY ENDPOINTS

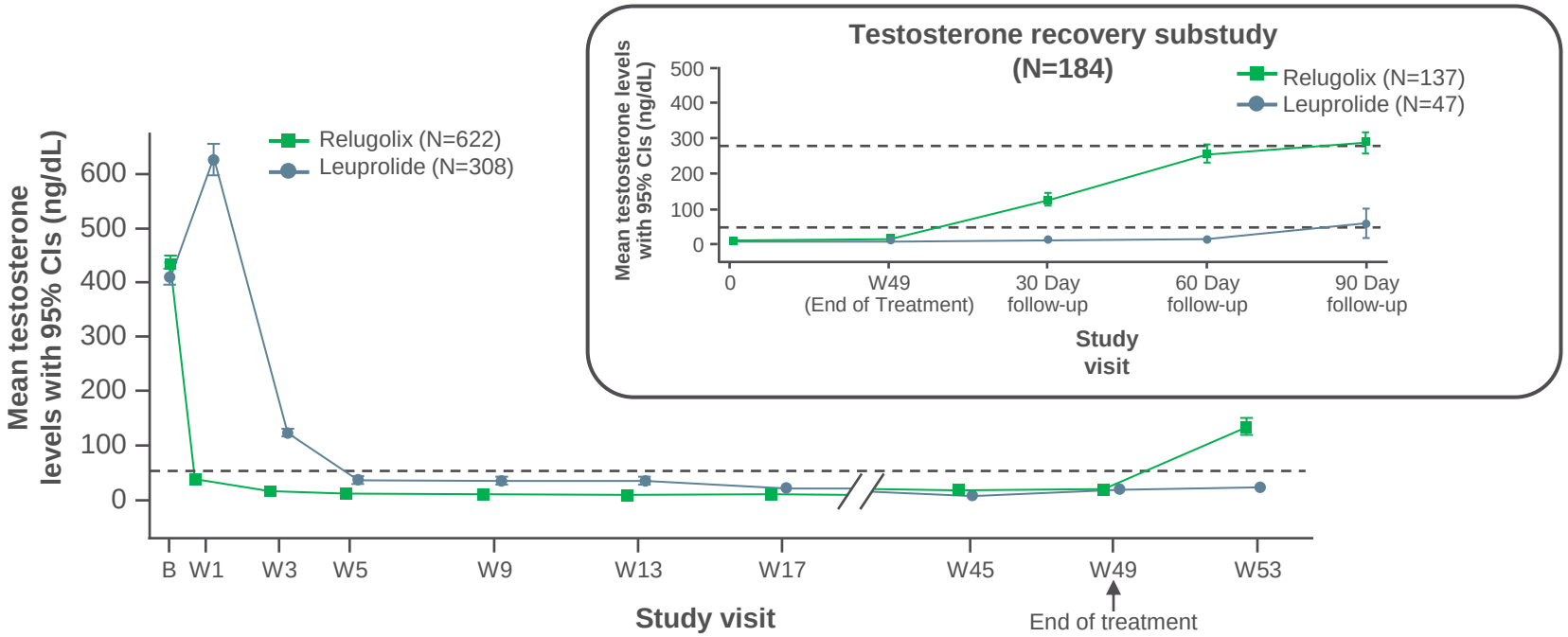
Secondary Endpoints	Relugolix (N=622) %	Leuprolide (N=308) %	P-value
Cumulative probability of testosterone suppression to <50 ng/dL at Day 4	56.0	0	<0.001
Cumulative probability of testosterone suppression to <50 ng/dL at Day 15	98.7	12.0	<0.001
Proportion of patients with PSA response at Day 15 followed with confirmation at Day 29	79.4	19.8	<0.001
Cumulative probability of profound testosterone suppression to <20 ng/dL at Day 15	78.4	1.0	<0.001
Mean of FSH level at end of week 24, IU/L	1.72	5.95	<0.001

CI, confidence interval; FSH, follicle stimulating hormone; IU, international unit; PSA, prostate specific antigen

Shore N, et al. ASCO 2020. Abstract #5602. Oral Presentation; Shore N, et al. N Engl J Med 2020. DOI: 10.1056/NEJMoa2004325

HERO STUDY: RESULTS

TIME COURSE OF TESTOSTERONE



50 ng/dL = castrate level; 280 ng/dL = lower limit of normal range B, baseline; W week

SAFETY SUMMARY

- Safety and tolerability profiles of relugolix and leuprolide were similar
- MACE were experienced by 2.9% relugolix group versus 6.2% leuprolide group

CI, confidence interval; MACE, major cardiovascular adverse events

Shore N, et al. ASCO 2020. Abstract #5602. Oral Presentation; Shore N, et al. N Engl J Med 2020. DOI: 10.1056/NEJMoa2004325

HERO STUDY: CONCLUSIONS

- Relugolix achieved castration as early as Day 4
- Compared to leuprolide, **relugolix achieved superiority** for:
  - **Sustained castration** rates
  - **Castration** (<50 ng/dL) and **profound castration** (<20 ng/dL) by Day 15
  - **PSA response** (decrease of >50%) by Day 15
- **Testosterone recovery within normal range** (54% vs 3%) at 90 days
- Relugolix treatment was **well tolerated**
  - **54% reduction in the risk of MACE with relugolix** treatment compared with leuprolide

Take home messages:

- Discuss the Pro's and con's of treatment options with patients (inc. cost-effectiveness and adherence)
- Consider relugolix in patients with severe hypersensitivity reactions to injections and significant cardiovascular history
- Possibly use as intermittent ADT given the fast testosterone recovery

ADT, androgen deprivation therapy; MACE, major cardiovascular adverse events; PSA, prostate specific antigen

Shore N, et al. ASCO 2020. Abstract #5602. Oral Presentation; Shore N, et al. N Engl J Med 2020. DOI: 10.1056/NEJMoa2004325

PHASE 2 TRIAL OF LENVATINIB PLUS PEMBROLIZUMAB FOR DISEASE PROGRESSION AFTER PD-1/PD-L1 IMMUNE CHECKPOINT INHIBITOR IN mccRCC

Lee C-H, et al.
ASCO 2020. Abstract #5008. Oral presentation

mccRCC, metastatic clear cell renal carcinoma

STUDY 111/KEYNOTE-146: BACKGROUND

RENAL CELL CARCINOMA COHORT

- Modulation of **vascular endothelial growth factor (VEGF)–mediated immune suppression** via angiogenesis inhibition **may augment the activity of immune checkpoint inhibitors (ICI)**[1]
- **Lenvatinib** (LEN), a multikinase **VEGF receptor inhibitor, plus everolimus is approved for advanced renal cell carcinoma** (RCC) after one prior anti-angiogenic therapy.[2] **Pembrolizumab** (PEM), an **anti-PD-1 antibody, plus axitinib is approved as first-line therapy of advanced RCC**[3]
- **Study 111/KEYNOTE-146** is a multicentre, open-label, single-arm phase 1b/2 trial evaluating the efficacy and safety of **LEN (20 mg/d)** in combination with PEM (200 mg intravenously every 3 weeks) in patients with selected solid tumours[4]
- **Results of the expansion cohort (n=104) of mccRCC** patients from study 111/KEYNOTE-146 who had progressed after ICI therapy are reported[4]
  - **Primary endpoint:** Objective response rate (ORR) at week 24 by irRECIST
  - **Secondary endpoints:** ORR, PFS, OS, safety and tolerability

ICI, immune checkpoint inhibitor; irRECIST, Immune-related Response Evaluation Criteria In Solid Tumours; LEN, Lenvatinib; mccRCC, metastatic clear cell renal cell carcinoma; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein-1; PEM, pembrolizumab; PFS, progression free survival; VEGF, vascular endothelial growth factor. 1. Taylor M, et al. J Clin Oncol 2020;38:1154-63; 2. Lenvatinib Prescribing Information Feb 2020; 3. Pembrolizumab Prescribing Information Apr 2020; 4. www.clinicaltrials.gov (NCT02501096)

STUDY 111/KEYNOTE-146: RESULTS

RENAL CELL CARCINOMA COHORT

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EFFICACY DATA

	irRECIST N=104
ORR (week 24), % (95% CI)	51 (41-61)
ORR, % (95% CI)	55 (45-65)
Best objective response, %	
Partial response	55
Stable disease	36
Progressive disease	5
Not evaluable	5
Median DOR, months (95% CI)	12 (9-18)
Median PFS, months (95% CI)	11.7 (9.4-17.7)
Median OS, months (95% CI)	NR (16.7-NR)

SAFETY DATA

	N=104
Any TRAEs	99%
TRAEs leading to treatment discontinuation	15%
TRAEs ≥ 20% of patients (any grade)*	
Fatigue	53%
Diarrhoea	46%
Proteinuria	39%
Hypertension	34%
Dysphonia	35%
Nausea	32%
Stomatitis	32%
Arthralgia	29%
Decreased appetite	28%
Palmar-plantar erythrodysesthesia syndrome	25%
Hypothyroidism	23%
Headache	22%

*Grade 5 TRAEs: upper gastrointestinal haemorrhage and sudden death

CI, confidence interval; DOR, duration of response; irRECIST, Immune-related Response Evaluation Criteria In Solid Tumours; NR, not reached; ORR, objective response rate; OS, overall survival; PFS, progression free survival; TRAE, treatment related adverse event

Lee C-H, et al. ASCO 2020. Abstract #5008. Oral Presentation

STUDY 111/KEYNOTE-146: CONCLUSIONS

RENAL CELL CARCINOMA COHORT

- **Lenvatinib plus pembrolizumab** demonstrated **promising anti-tumour activity in patients with mccRCC** with disease progression following PD-1/PD-L1 ICI therapy
- **Adverse event profile** of the combination treatment was **consistent with other studies**. No new safety signals were detected
- A phase 3 study is evaluating the combination for first-line treatment in advanced RCC (NCT02811861)

Take home messages:

- Consider Lenvatinib plus pembrolizimub in patients with a clear cell histology following disease progression after first line ICI therapy
- For patients who have tolerated IO very well, this allows continuation of IO by combining with a different TKI

ICI, immune checkpoint inhibitor; IO, immuno-oncology; mccRCC, metastatic clear cell renal cell carcinoma; PD-1, programmed cell death-1; PD-L1, programmed death ligand-1

Lee C-H, et al. ASCO 2020. Abstract #5008. Oral Presentation

IMPACT OF AN IO EDUCATION/MONITORING PROGRAM ON PATIENTS SELF-EFFICACY AND ADVERSE EVENT REPORTING FROM IMMUNE CHECKPOINT INHIBITORS

Cheema PK, et al.
ASCO 2020. Abstract #2032. Poster presentation

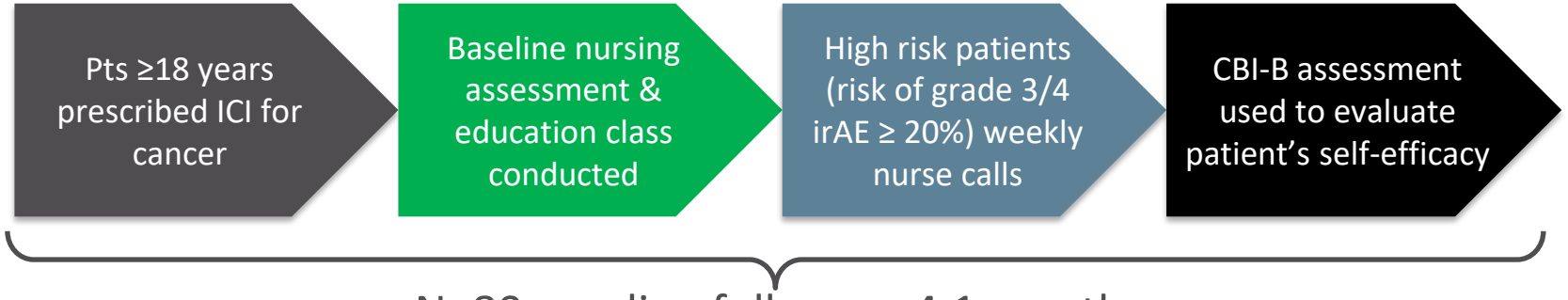
IO, immuno-oncology

BACKGROUND

- Use of **immune checkpoint inhibitors** (ICIs) is associated with serious adverse events related to excessive immune activation, known as **immune-related adverse events (irAEs)**[1]
- **Communication** of these irAEs **to patients is important** to aid early detection and management

METHODS

- A standard nursing immuno-oncology (IO) education and monitoring program was implemented at a single Canadian centre between May 2018-Dec 2019



CBI-B, cancer behaviour inventory-brief version; ICI, immune checkpoint inhibitors; IO, immuno-oncology; irAEs, immune-related adverse events

1. Connolly C, et al. Front Oncol 2019; 9: doi: 10.3389/fonc.2019.00530; 2. Cheema PK, et al. ASCO 2020. Abstract #2032. Poster Presentation

RESULTS

Baseline Characteristics	(N=80)
Median age	69 yrs
Males	70% (56)
English as first language	66% (53)
Highest level of education	
Elementary	19% (15)
High school	30% (24)
Trade diploma	26% (21)
Post-secondary	21% (17)
Limited cancer health literacy	41% (33)
ICI prescribed	
Monotherapy anti-PD1/PDL1	70% (56)
Nivolumab/ipilimumab combination	13% (10)
Anti-PD-1/PD-L1 + CT/other therapies	17% (14)
Cancer diagnosis	
NSCLC	55% (55)
Melanoma	19% (15)
RCC	9% (6)
Other	5% (4)

- Significant improvement in CBI-B scores pre- and post-assessment/education ($p<0.001$) which was maintained over time

	N=80 %
Patients ≥ 1 irAE	43
irAE grade 1/2 (when detected)	65
irAE requiring ER visit (n=3)	3.75
Method of detection of irAE	
Patient self-reporting	62
Followed by proactive calls	27
Rate of discontinuation of ICI	8.8

CBI-B, cancer behaviour inventory-brief version; CT, chemotherapy; ER, emergency room; ICI, immune checkpoint inhibitors; irAE, immune-related adverse event; NSCLC, non-small cell lung cancer; PD-1, Programmed cell death protein 1; PD-L1, Programmed cell death ligand 1; RCC, renal cell carcinoma

Cheema PK, et al. ASCO 2020. Abstract #2032. Poster Presentation

CONCLUSIONS

- A **standardised IO baseline assessment, education and monitoring program resulted in improved patient self-efficacy**
  - Most irAEs were detected by self-reporting and proactive calls

- This IO program can be a model for other oncology programs

Take home messages:
- With a diverse patient population, it is key is to incorporate a standardised nursing assessment and education program with proactive follow up to improve patients understanding of treatment toxicities

IO, immuno-oncology; irAE, immune-related adverse event
Cheema PK, et al. ASCO 2020. Abstract #2032. Poster Presentation

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