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# MEETING SUMMARY
# ASCO 2019, Chicago, USA


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# NEUROENDOCRINE TUMOUR UPDATE

# DISCLAIMER

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# TOP 3 HIGH-IMPACT NEUROENDOCRINE PRESENTATIONS AT ASCO AND AACR 2019

# RESULTS OF ALLIANCE (A021202): PHASE II STUDY OF PAZOPANIB VS PLACEBO IN PROGRESSIVE CARCINOID TUMOURS

**Bergsland, et al. ASCO 2019 Abstract #4005**

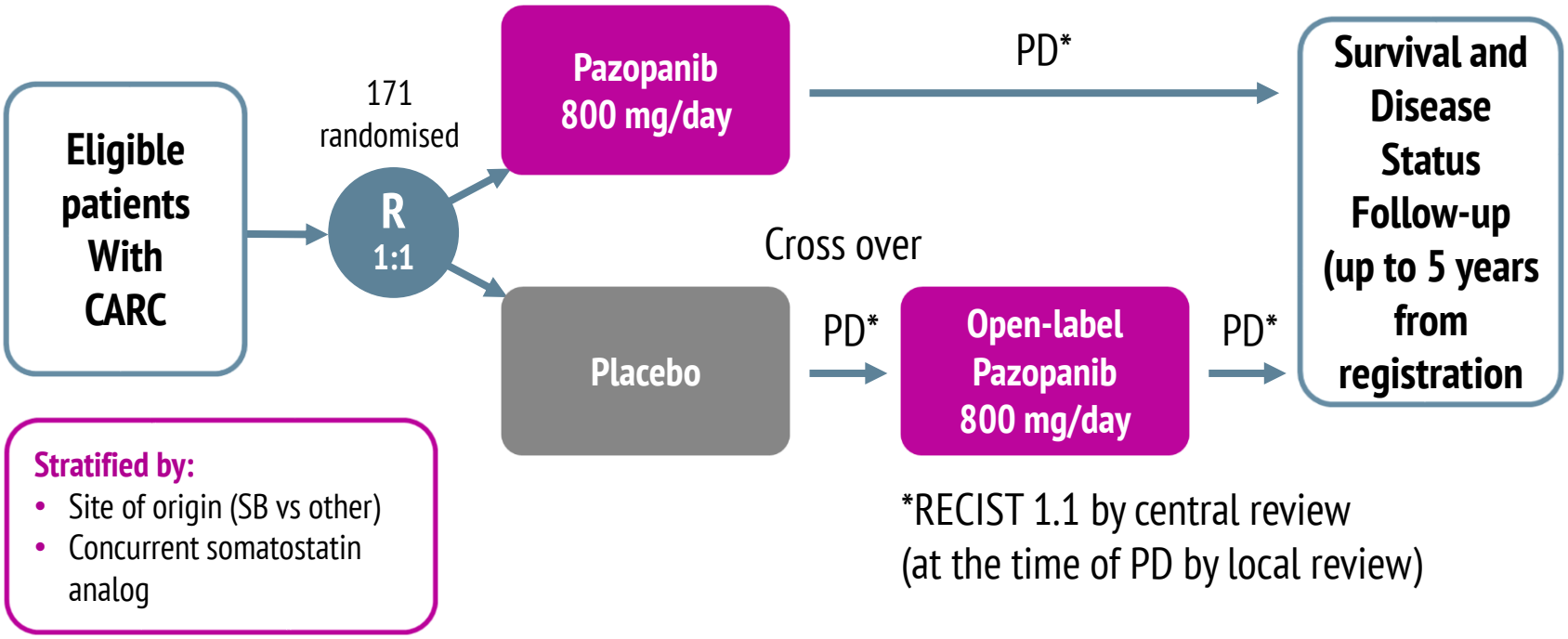
# BACKGROUND

- Currently available treatments for advanced carcinoid tumours eventually lead to resistance:
  - Lanreotide
  - Everolimus
  - Lu177 dotatate
- Additional treatment options are therefore required
- VEGF and its receptors are expressed in gi/panNETs
- ALLIANCE study evaluates the effect of Pazopanib, a multi-targeted receptor tyrosine kinase inhibitor, in advanced carcinoid tumours

giNET, gastrointestinal neuroendocrine tumour; panNET, pancreatic neuroendocrine tumour; VEGF, vascular endothelial growth factor

Bergsland, et al. Presented at ASCO 2019. Abstract #4005

# ALLIANCE STUDY DESIGN




CARC, carcinoid carcinomas; PD, progressive disease; SB, small bowel

Bergsland, et al. Presented at ASCO 2019. Abstract #4005

# ALLIANCE ENDPOINTS

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## PRIMARY: PFS BY CENTRAL REVIEW

### Key Secondary Endpoints

- Overall survival
- Objective response rate
- Duration of response
- Time to treatment failure
- PFS (local review)
- Safety and tolerability

### Other Secondary Endpoints

- Quality of Life
- Angiome profiling – correlation with response/toxicity
- Other radiographic endpoints

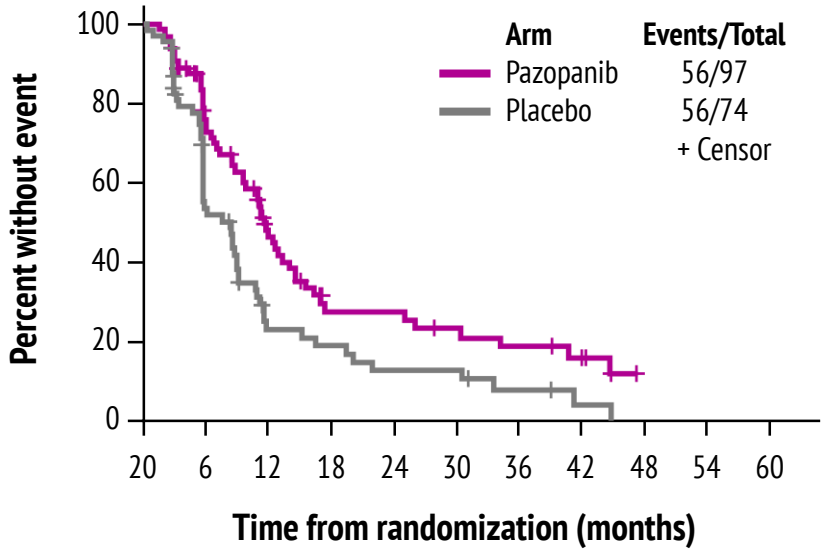
PFS, progression free survival

Bergsland, et al. Presented at ASCO 2019. Abstract #4005

# ALLIANCE RESULTS

## PROGRESSION FREE SURVIVAL (CENTRAL REVIEW)

- PFS 11.6 months (pazopanib) vs 8.5 months (placebo)




**Patients at risk:**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Pazopanib | 52 | 29 | 13 | 13 | 10 | 8 | 6 | 0 |
| Placebo | 33 | 11 | 9 | 6 | 6 | 3 | 1 | 0 |

| | Pazopanib (N=97) | Placebo (N=74) |
|---|---|---|
| No. of events | 56 | 56 |
| 12 mo. PFS, % (90% UCB*) | 46.4 (54.7) | 22.9 (31.4) |
| **Median PFS, mo. (90% UCB)** | **11.6 (13.0)** | **8.5 (8.9)** |
| **HR (90% UCB)** | **0.53 (0.69)** | **REF** |
| **Stratified Log-Rank P-value = 0.0005** | | |
| Adj. HR** (90% UCB) | 0.57 (0.74) | REF |
| Adjusted Log-Rank P-value = 0.0020 | | |

**Gender, functional tumor, age and stratification factors (consurrent SSA, site of primary)

HR, hazard ratio; PFS, progression free survival; REF, reference; SSA, somatostatin analogue; UCB, upper confidence bound

Bergsland, et al. Presented at ASCO 2019. Abstract #4005

# SUMMARY

- **Pazopanib improves PFS** in patients with progressive carcinoids
- No difference in Overall Survival between treatment arms
  - Confounded by crossover
- QoL assessment similar between both arms
- **Expected AE profile**; overall increase in grade ⩾3 AEs
- Potential benefit of pazopanib to be considered alongside toxicity

AE, adverse event; PFS, progression free survival; QoL, quality of life

Bergsland, et al. Presented at ASCO 2019. Abstract #4005

# FINAL RESULTS OF TALENT: A PHASE II MULTICOHORT STUDY OF LENVATINIB IN PATIENTS WITH G1/G2 panNETs AND giNETs

**Capdevila, et al. ASCO 2019 Abstract #4106**

panNETs, pancreatic neuroendocrine tumours; giNETs, gastrointestinal neuroendocrine tumours

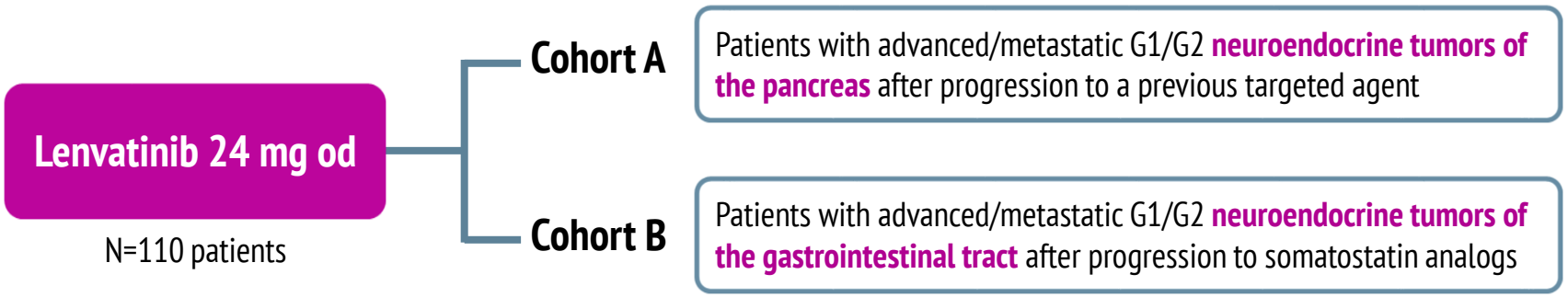
# BACKGROUND

- There are **limited treatment options** for patients with advanced well-differentiated **(G1/G2) NETs**
- **Lenvatinib is a multikinase inhibitor** with potent affinity against VEGFR1-3 and FGFR1-4 that may increase efficacy and revert primary and acquired resistance to TA
- TALENT was a phase II study to evaluate the efficacy of lenvatinib in panNETs and giNETs
- Final results, including subgroup analyses are presented here

FGFR, fibroblast growth factor receptor; giNET; gastrointestinal neuroendocrine tumour; NET, neuroendocrine tumour; panNET, pancreatic neuroendocrine tumour; TA, targeted agents; VEGFR, vascular endothelial growth factor receptor

Capdevila, et al. ASCO 2019. Abstract #4106

# TALENT STUDY DESIGN




- **Primary endpoint:** ORR by RECIST
- **Secondary endpoint:** PFS, OS and safety

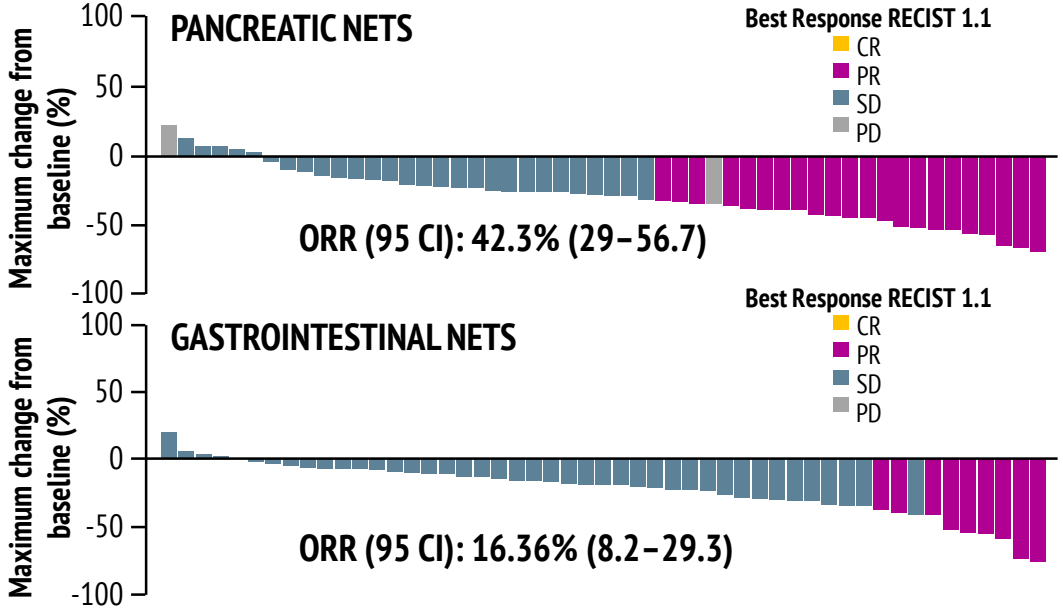
od, one a day; ORR, overall response rate; OS, overall survival; PFS, progression free survival

Capdevila, et al. ASCO 2019. Abstract #4106

# TALENT RESULTS

- ORR in panNET: 42.3%; ORR in giNET: 16.3%
- Median follow up 19 months
- In the subgroup analysis, all patients obtained the same benefit in PFS and ORR

## PRIMARY ENDPOINT




## SECONDARY ENDPOINTS

| | PFS (mo) | OS (mo) |
|---|---|---|
| PanNETS | 15.5 | 29.2 |
| giNETS | 15.4 | NR |

## SAFETY

- Most frequent G3/4 AEs: hypertension (22%), fatigue (11%) and diarrhoea (11%)
- Dose reductions required in 91.8% of patients (median dose 20 mg)

AE, adverse event; CR, complete response; giNET, gastrointestinal neuroendocrine tumour; ORR, overall response rate; OS, overall survival; panNET, pancreatic neuroendocrine tumour; PD, progressive disease; PFS, progression free survival; PR, partial response; SD, stable disease

Capdevila, et al. ASCO 2019. Abstract #4106

# SUMMARY

- **Lenvatinib** showed **promising PFS and OS benefit** in a pre-treated population

- This benefit **was evident across all subgroups** studied

PFS, progression free survival; OS, overall survival

Capdevila, et al. ASCO 2019. Abstract #4106

# RESULTS OF DART: A PHASE II BASKET TRIAL OF NIVOLUMAB AND IPILIMUMAB COMBINATION IN RARE TUMOURS (NEUROENDOCRINE COHORT)

**Patel, et al. AACR 2019 Abstract #CT039**

# BACKGROUND

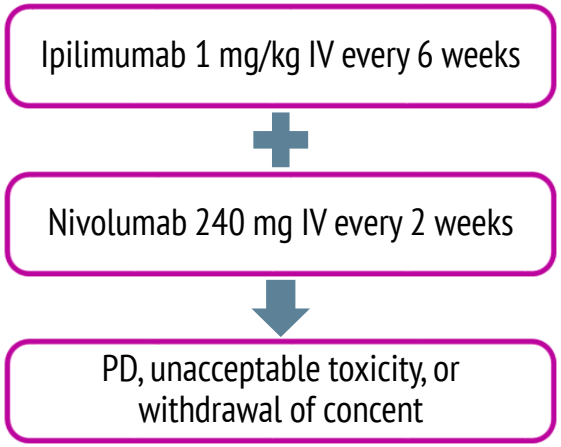
- **Immune checkpoint inhibitors**, such as anti-CTLA-4 and anti-PD-1 blockade, have **improved clinical outcomes in various tumours**
- There is a **lack of data** regarding these agents **in rare cancers**
- The **DART** trial, investigated the effects of **ipilimumab and nivolumab** on various rare tumours
- The data from the **neuroendocrine cohort** was **presented at AACR 2019**

CTLA-4, cytotoxic T-lymphocyte–associated antigen 4; PDL-1, programmed death-ligand 1

Patel, et al. Presented at AACR 2019. Abstract #CT039

# DART STUDY DESIGN

- Open label, phase II, basket trial
- Multiple cohorts of rare tumours included
- Concurrent combination immunotherapy:
  - Ipilimumab
  - Nivolumab
- Nivolumab monotherapy allowed for patients with severe toxicity on combination
- Treatment cycle of 6 weeks
- Imaging assessments every 12 weeks




PD, progressive disease

Patel, et al. Presented at AACR 2019. Abstract #CT039

# DART ENDPOINTS

## NEUROENDOCRINE COHORT

- 32 eligible patients
  - Does NOT include pancreatic NET (separate study cohort)
  - 1 patients re-stratified to PanNET cohort
- 56% (n=18) had high-grade carcinoma
- Most common sites: 47% giNET (n=15) and 19% lung (n=6)
- Median number of prior lines of therapy: 2

**Primary Endpoint**

- Overall response rate by RECIST

**Secondary Endpoints**

- Progression free survival
- Overall Survival
- Stable disease > 6 months
- Toxicity

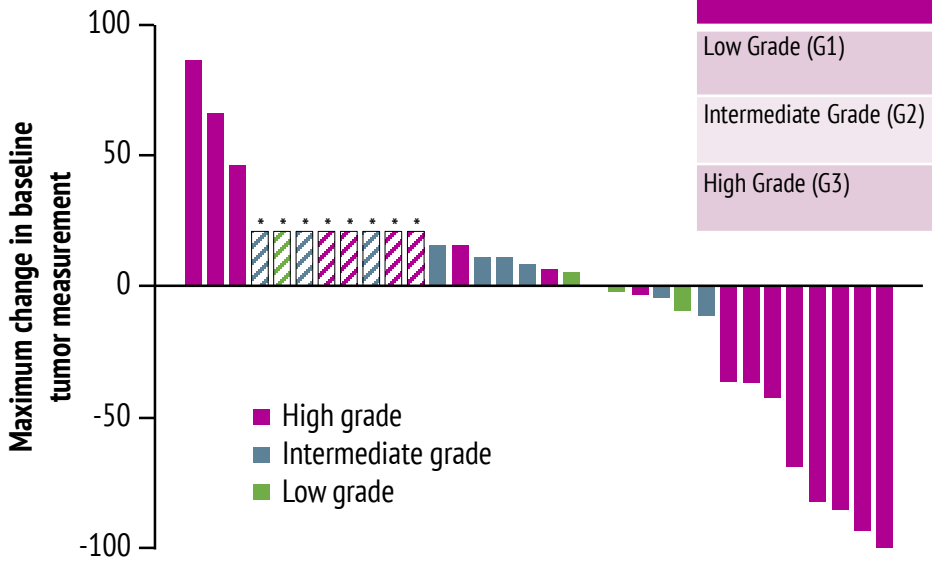
giNET, gastrointestinal neuroendocrine tumour; NET, neuroendocrine tumour; panNET, pancreatic neuroendocrine tumour

Patel, et al. Presented at AACR 2019. Abstract #CT039

# DART RESULTS

- ORR 44% in high grade NEC independent of primary site
  - 18 out of 32 patients were high grade NEC
- OS was > 11 months; 6-month PFS was 31%

## Response Rate by Tumor Grade of Neuroendocrine Neoplasm




| Grade | Gastrointestinal NET (excluding pancreas) | Lung and Thymus |
|---|---|---|
| Low Grade (G1) | <2 mitoses/10 HPF AND/OR <3% Ki-67 index | <2 mitoses/10 HPF AND no necrosis |
| Intermediate Grade (G2) | 2–20 mitoses/10 HPF AND/OR 3–20% Ki-67 index | <–10 mitoses/10 HPF AND/OR foci of necrosis |
| High Grade (G3) | >20 mitoses/10 HPF AND/OR >20% Ki-67 index | >10 mitoses/10 HPF |

HPF, high power fields; NEC, neuroendocrine carcinoma; NET, neuroendocrine tumour; ORR, overall response rate; OS, overall survival

Patel, et al. Presented at AACR 2019. Abstract #CT039

# SUMMARY

- Patients with **high grade NEC derived clinical benefit** from the **combination treatment**
- No significant activity in low grade NECs
- Ipilimumab plus nivolumab was **well tolerated**
  - Most common AEs: fatigue (30%) and nausea (27%)
  - Mot common grade 3-4 AEs: ALT (9%) and AST (6.3%) elevations
  - No grade 5 toxicities
- Further study with dual CTLA-4 and PDL-1 inhibition is warranted in high grade NEC

AE, adverse event; CTLA-4, cytotoxic T-lymphocyte–associated antigen 4; NEC, neuroendocrine carcinoma; PDL-1, programmed death-ligand 1

Patel, et al. Presented at AACR 2019. Abstract #CT039

# CONCLUSIONS

- Recent data is encouraging and after many years provides optimism for treatment options for high grade NEC

- Further randomized trials are warranted

NEC, neuroendocrine carcinoma

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