2021 ASCO ANNUAL MEETING

ORAL SELPERCATINIB IN PEDIATRIC PATIENTS WITH ADVANCED *RET*-ALTERED SOLID OR PRIMARY CNS TUMORS: PRELIMINARY RESULTS FROM THE PHASE 1/2 LIBRETTO-121 TRIAL

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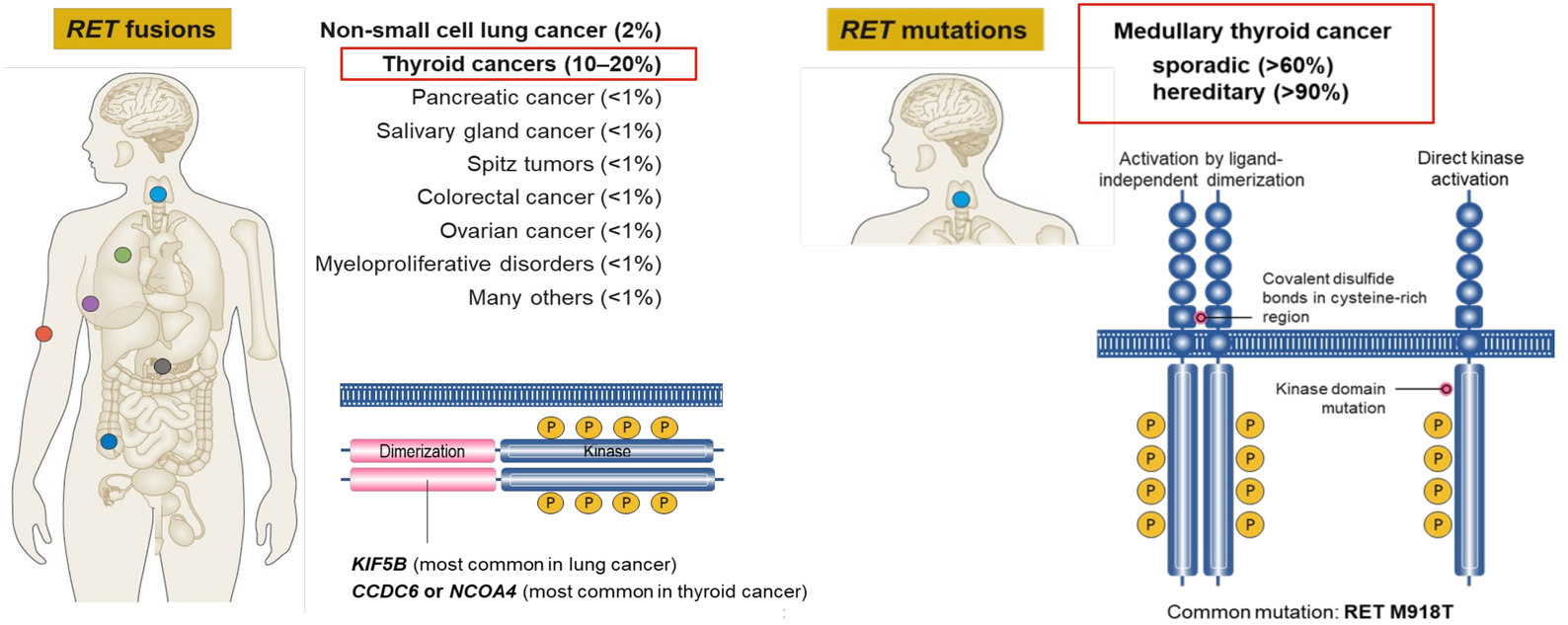
Activating *RET* alterations are actionable oncogenic drivers

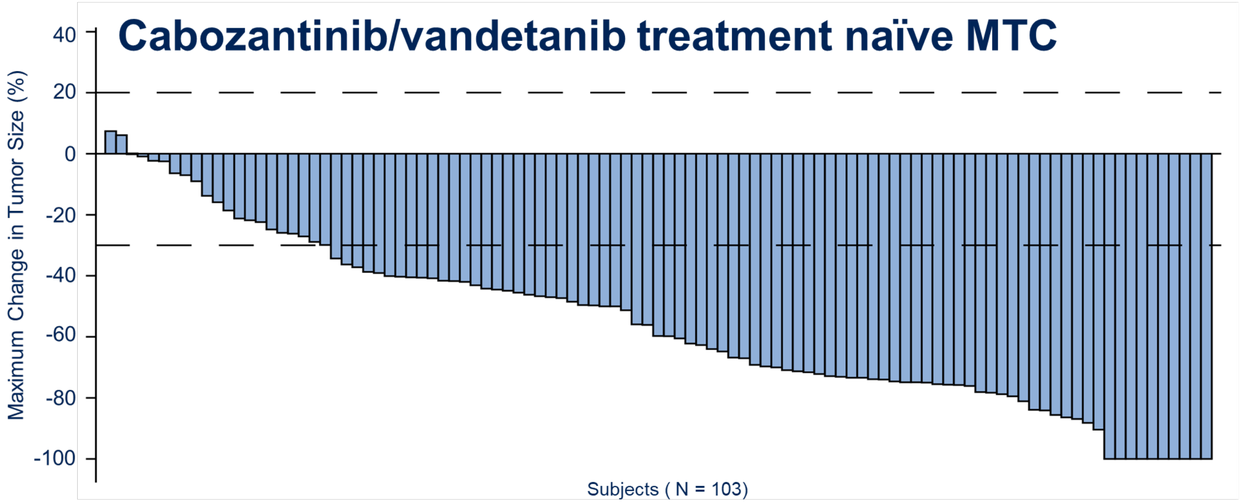


- RET fusions are the most common actionable alteration in children with PTC; the majority of children with MTC have germline RET mutations/MEN2 syndromes
- In infants and children, RET fusions have also been occasionally reported in patients with various sarcoma subtypes
- Selpercatinib is a highly selective and potent RET inhibitor with CNS activity

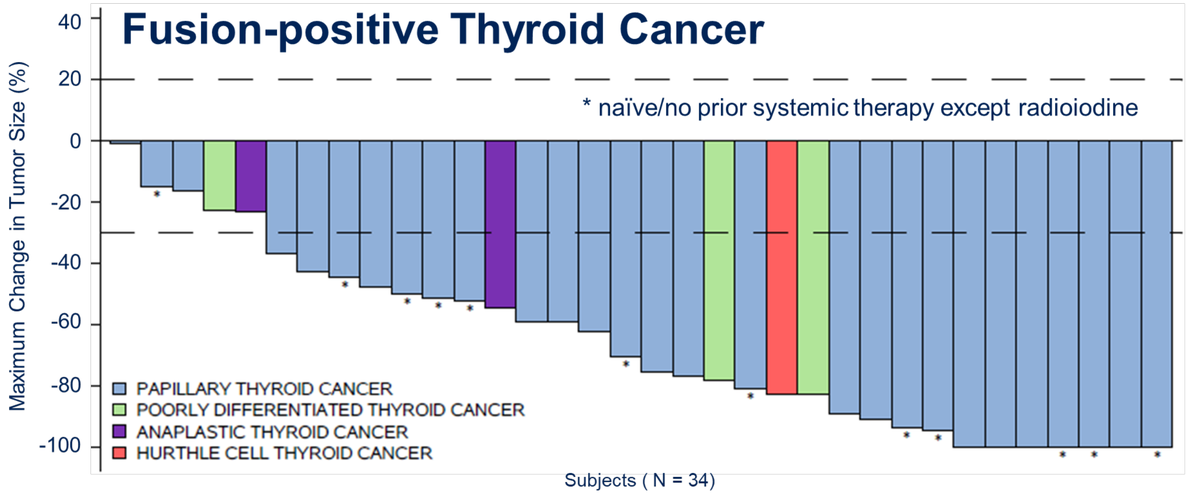
Pekova et al. Thyroid 2020 Dec 2020; 30(12):1771-1780; Brandi et al. J Clin Endocrinol Metabl 2001 Dec;86(12):5658-71; Ortiz et al. JCO Precis Oncol 2020; 4: PO.19.00401; Drilon et al. Nat Rev Clin Oncol 2018;15:151–67; Kato et al. Clin Cancer Res 2017; 23:1988–97; Pietrantonio et al. *Ann Oncol* 2018;Mar 10; Su et al. *PLoS One* 2016;11(11)

Efficacy of Selpercatinib in *RET*-Altered Thyroid Cancers

- Selpercatinib is efficacious in adults with *RET* mutant MTC and *RET* fusion-positive thyroid cancer
- MTC biochemical response (calcitonin, CEA) typically precedes maximum radiographic response
- The efficacy and safety of selpercatinib in adults support the evaluation of selpercatinib in pediatric patients with *RET*-altered cancers



ORR 71.4% (95% CI: 62.1-79.6)



ORR 82.4% (95% CI: 65.5-93.2)

Sherman E, et al. ASCO Annual Meeting 2021

LIBRETTO-121 Study Design

Phase 1 Dose Escalation / Confirmation

Dose Level 1
92 mg/m^2 BID

Phase 2 Expansion Cohorts

Cohort 1	Cohort 2	Cohort 3	Cohort 4
RET fusion-positive solid tumor with measurable disease	*RET*-mutant MTC with measurable disease	*RET* fusion-positive CNS tumor with measurable disease	*RET* alteration but not eligible for Cohorts 1-3[a]

Study Design

- LIBRETTO-121 (NCT03899792) is a multicenter phase 1/2 trial in pediatric patients with advanced, *RET*-altered solid or CNS tumors
- Dosing started at 92mg/m^2 BID equivalent to the adult dose of 160mg BID
- Age ≥6 months to ≤21 years (≥12 years in EU and Canada)
- RP2D confirmed separately for patients <2 years and ≥2 years of age
- Primary Endpoints: MTD/RP2D (Phase 1), ORR (Phase 2)

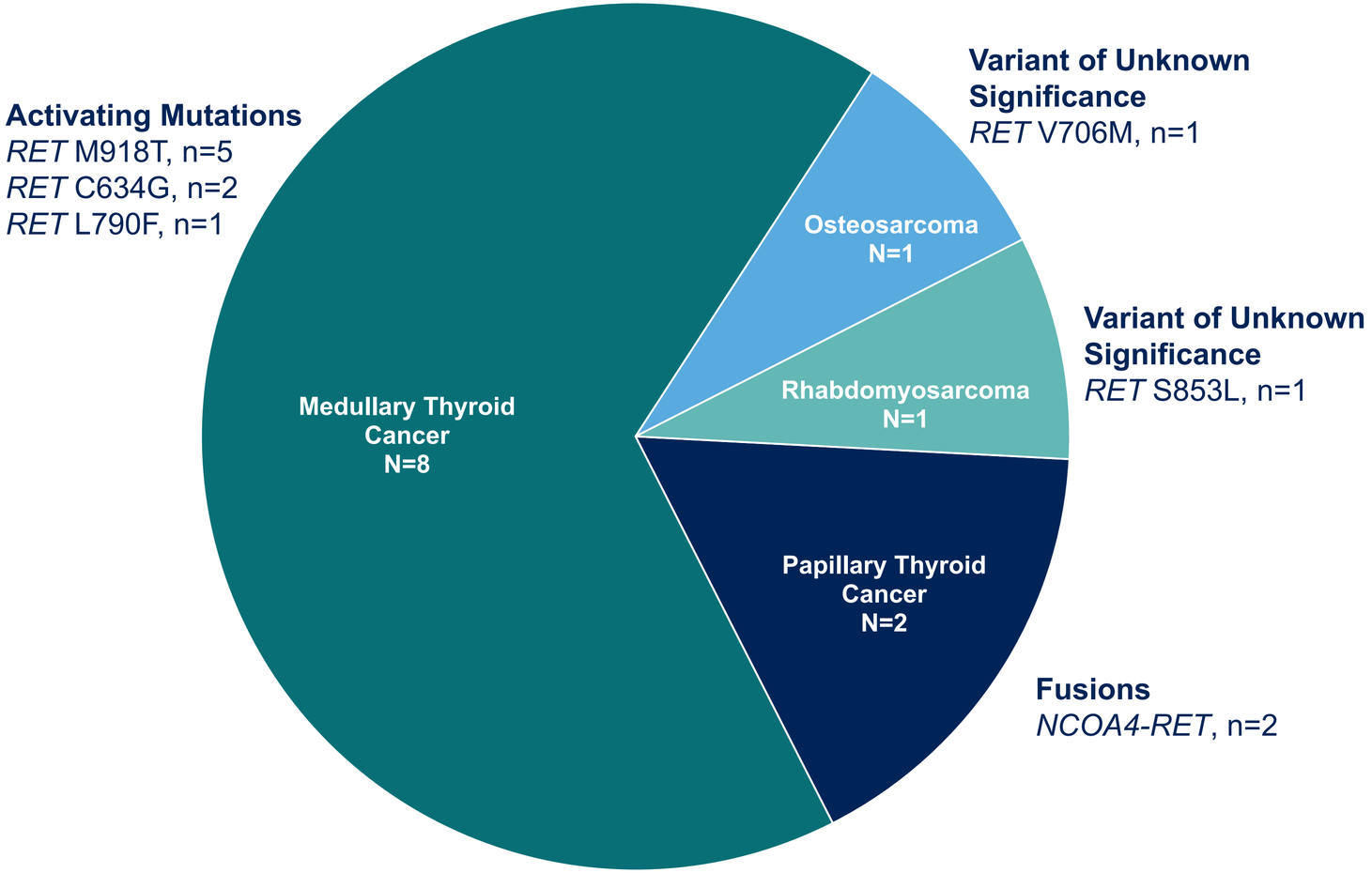
[a]on the basis of RET alteration characteristics or absence of RECIST measurable disease
Abbreviations: CNS = central nervous system; MTD = maximum tolerated dose, ORR = overall response rate, RP2D = recommended phase 2 dose

Data cut performed on 30 March 2021

Baseline Characteristics

Characteristic	Total N=12
Age, years	
Median (Range)	14 (2-20)
Age Group, n	
6 mo – 2 yrs	1
>2 yrs – <12 yrs	3
12 yrs – <18 yrs	5
18 yrs - 21 yrs	3
Gender, n	
Female	6
Male	6
Disease Status at Study Entry	
Metastatic	9
Locally Advanced	3
Prior Systemic Therapy	3
Prior Radiotherapy	4
Prior Surgery	9
Karnofsky / Lansky Performance	
50-60	4
80	1
100	7

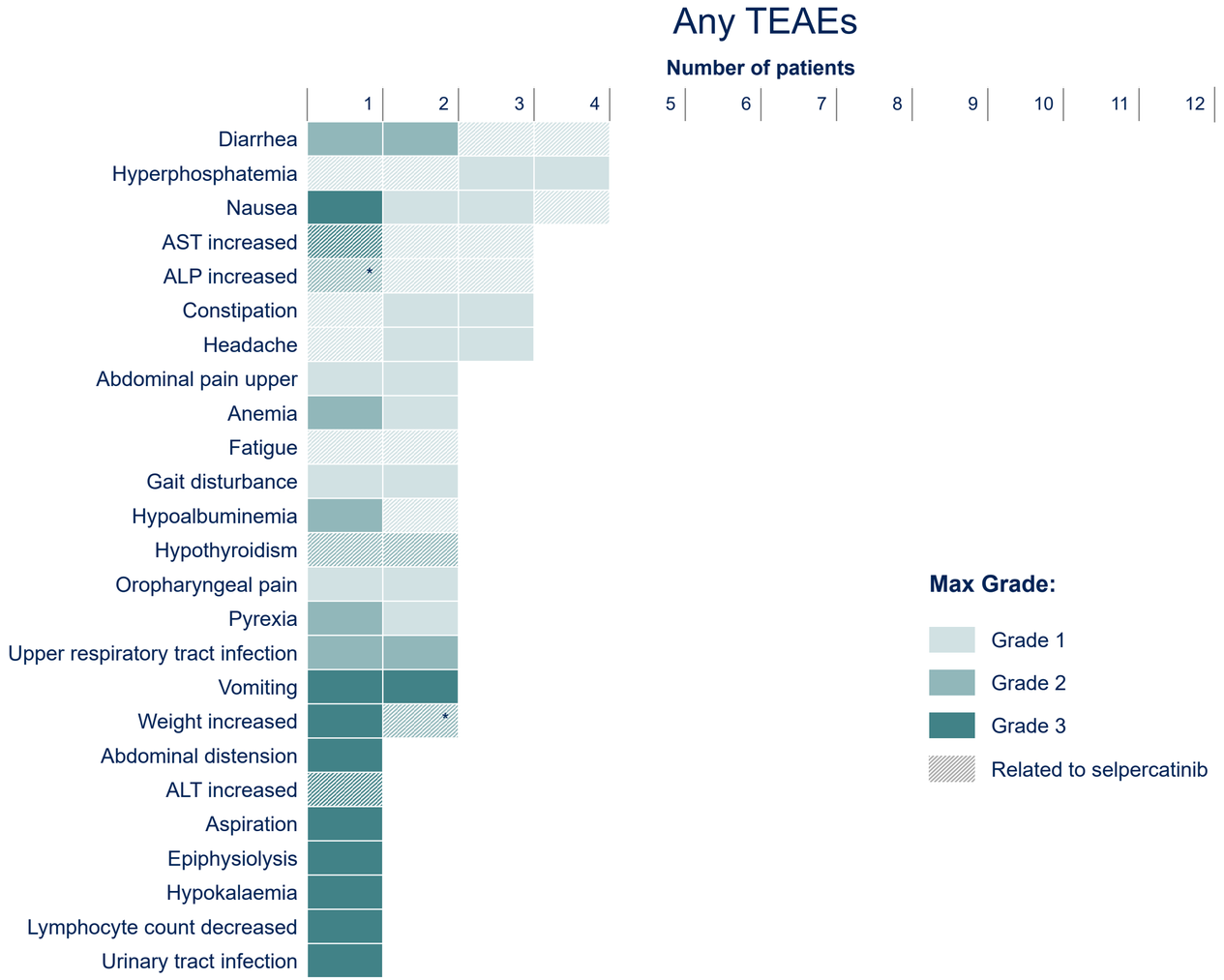
Primary Diagnosis



Data cut performed on 30 March 2021

Safety

- No DLTs at dose level 1 (92mg/m^2), expansion cohorts opened at this RP2D
- 1 patient discontinued treatment due to PD, 1 due to patient non-compliance and 1 due to AEs[a]

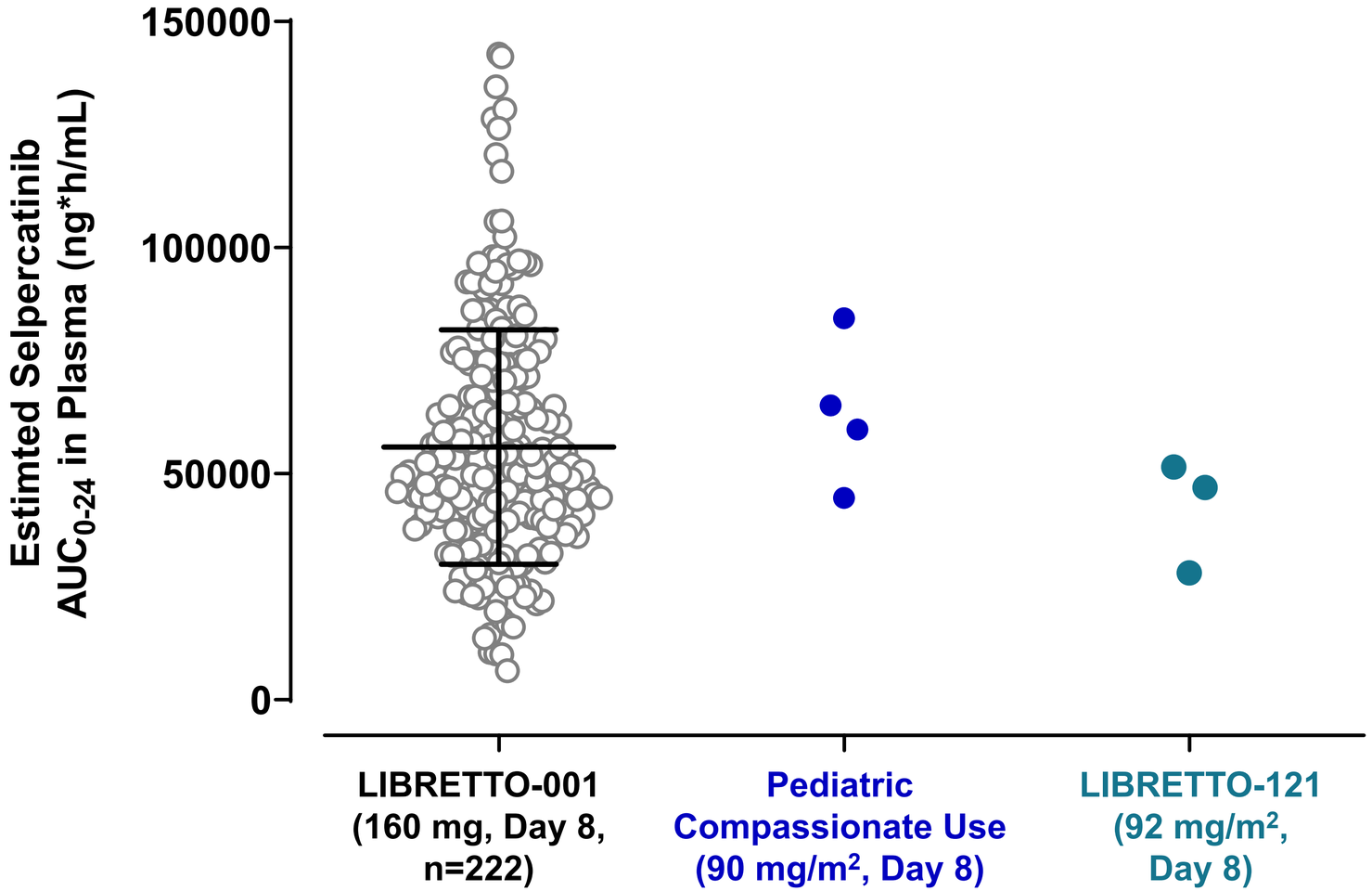


Any TEAEs occurring in ≥2 Patients or ≥G3 TEAEs occurring in any patient

* A subject had the corresponding TEAE up to G2, but selpercatinib-related AE was G1

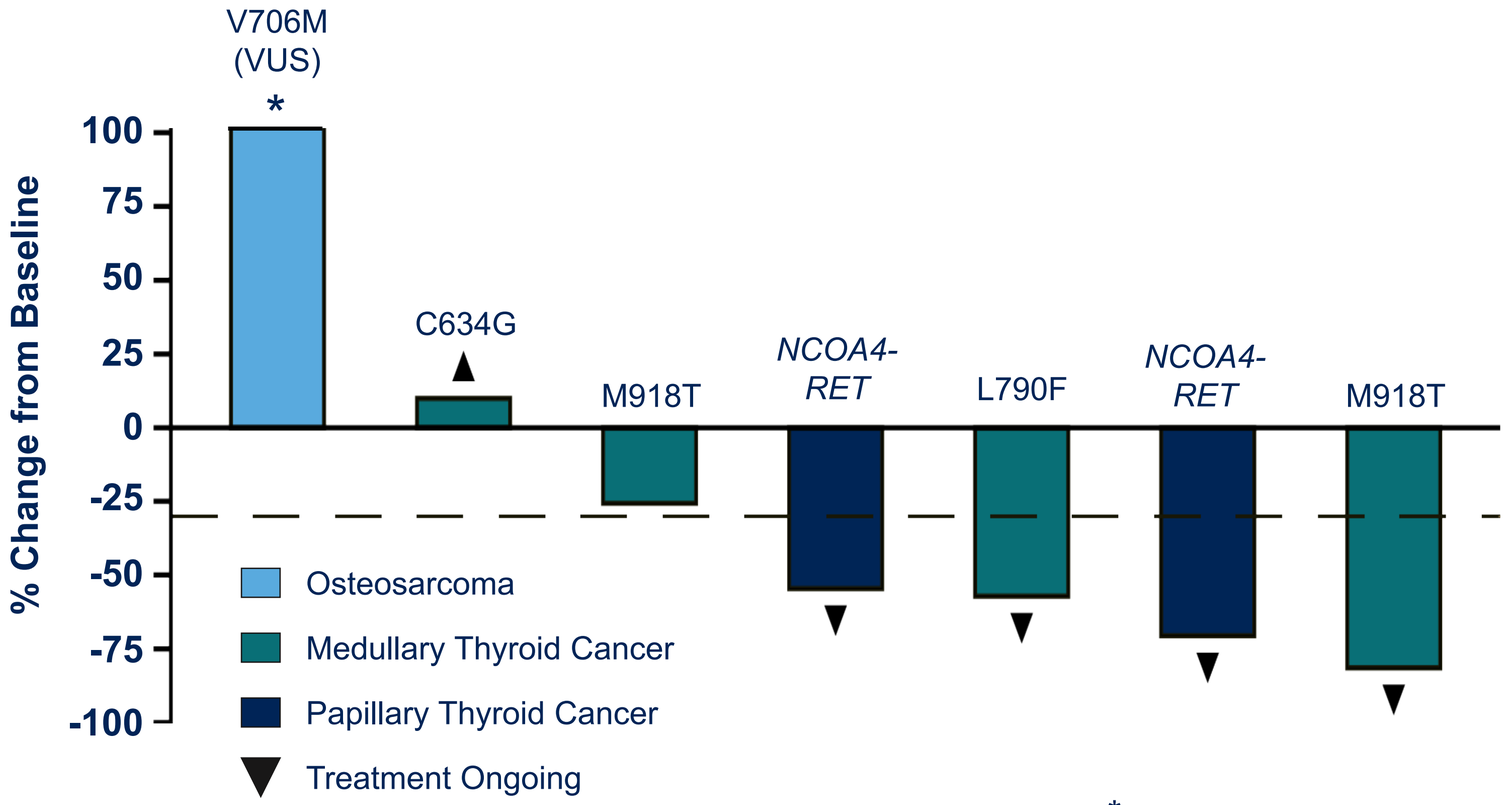
[a]No evidence shows that the AEs are related to selpercatinib
Data cut performed on 30 March 2021

Pharmacokinetics of Selpercatinib in Pediatric Patients



- PK results in participants, while limited, are consistent with results in adults

Tumor Response by Cancer Type



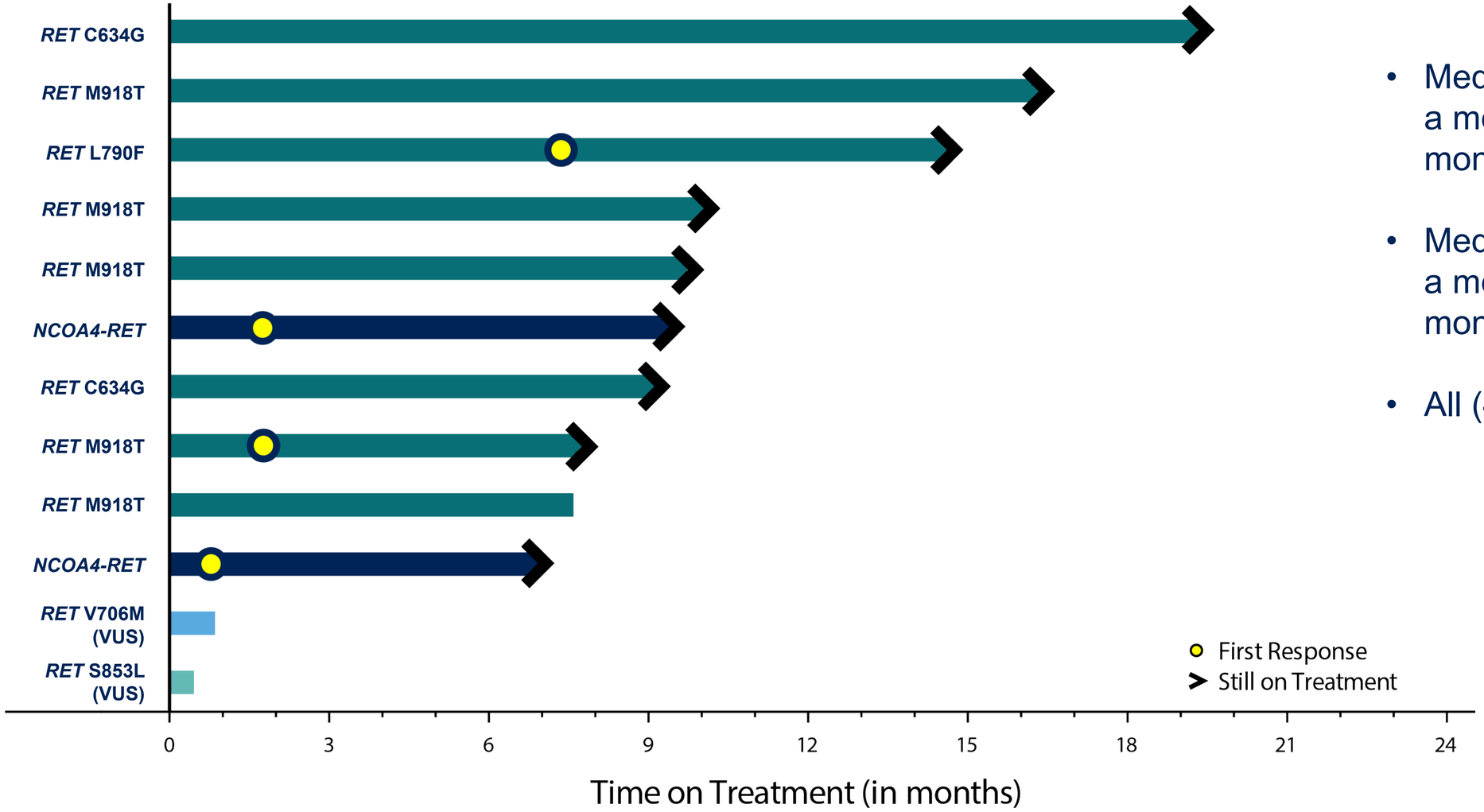
* +121% change from baseline

Best Objective Response by Investigator[a]	RECIST Measurable N=8
CR	0
PR	4
SD	2
PD	1
NE	1[c]
Objective Response Rate, % [95% CI]	**50 [16-84]**
Clinical Benefit Rate[b], % [95% CI]	**75 [35-97]**

The waterfall plot includes only patients with measurable disease. One patient is not included due to absence of post-baseline tumor assessment documentation. Four patients are not included because they had non-measurable disease. All four patients had best objective response of Non-CR/Non-PD.

[a]PR, all partial responses were confirmed by a second scan ≥28 days after the initial response; [b]Clinical Benefit Rate (%) is defined as the proportion of patients with Best Objective Response of CR, PR or SD; [c]Patient died due to PD; however, was classified as NE due to absence of post-baseline tumor assessment documentation. All efficacy data per investigator assessment.
Data cut performed on 30 March 2021.

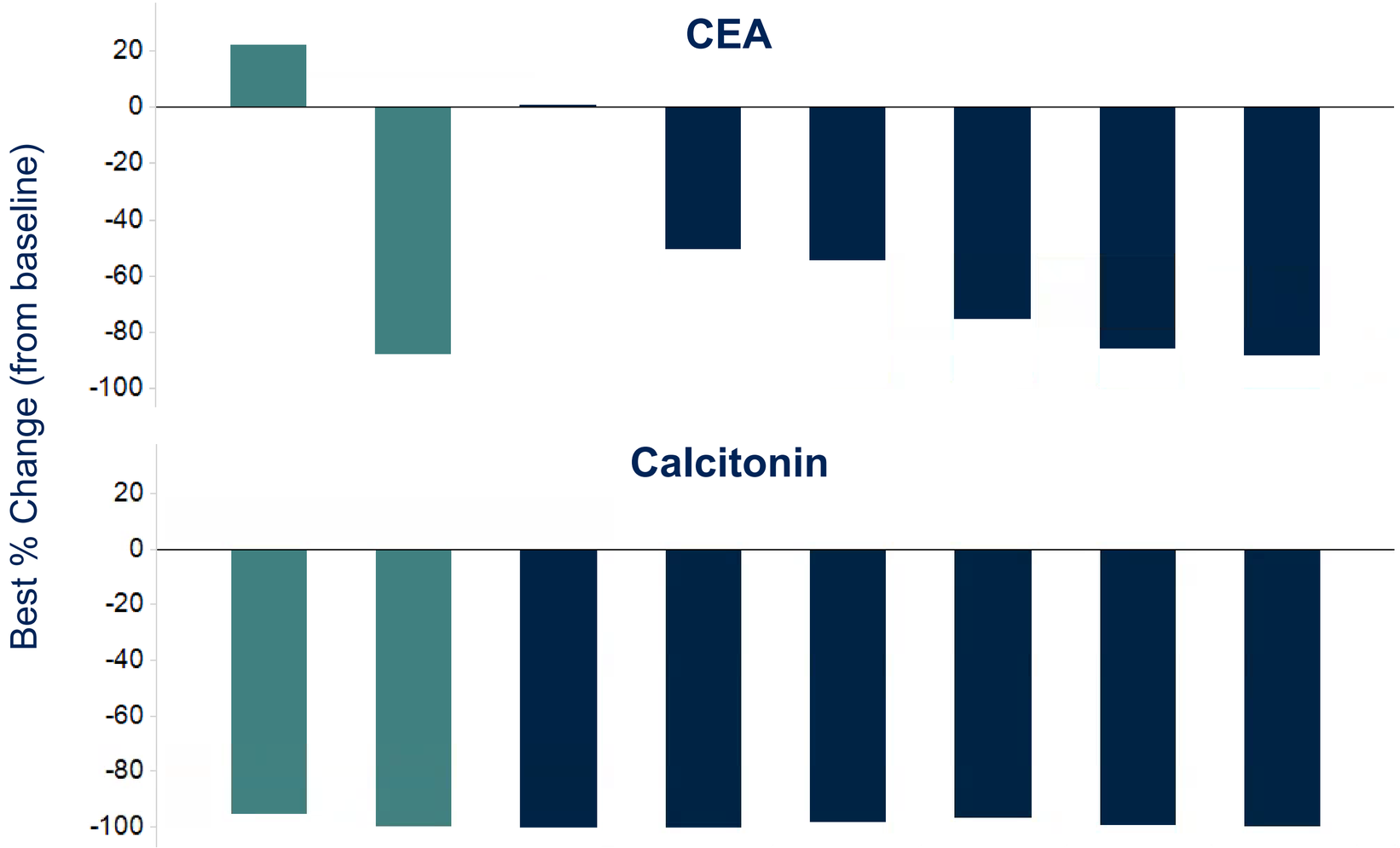
Duration of Selpercatinib Treatment



- Median PFS was not reached at a median follow-up time of 8 months from the first dose
- Median DOR was not reached at a median follow-up time of 5 months from initial response
- All (4/4) responses ongoing

Data cut performed on 30 March 2021

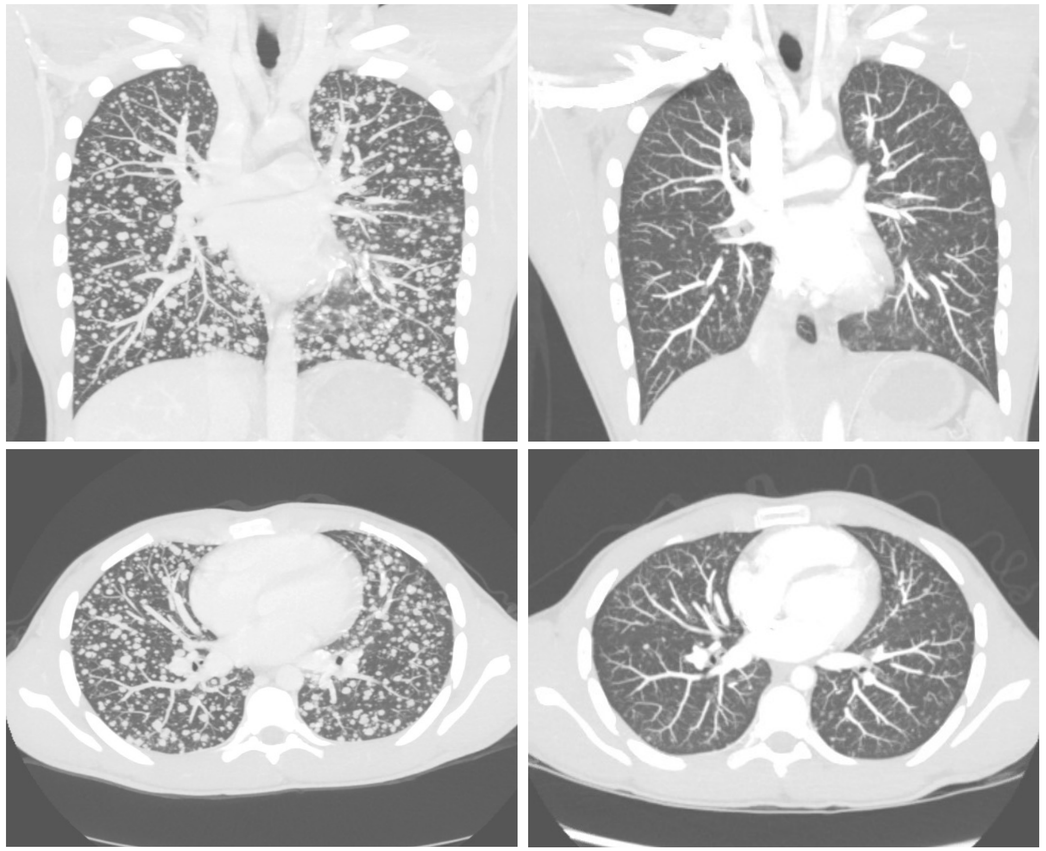
Biochemical Response in MTC Patients Regardless of Radiographic Response



Data cut performed on 30 March 2021

Case Study: 15-year-old with PTC

- **Diagnosis:**
  - *NCOA4-RET* Fusion-positive PTC
- **Prior therapy:**
  - Total thyroidectomy and left lateral neck dissection in 2016
  - Radioactive iodine in 2016 and 2018
- **Selpercatinib started 2020**
  - Reached PR (investigator assessed) at 1.7 months of treatment, treatment ongoing at 9.4 months
  - Related AE of G1 rash and weight decreased

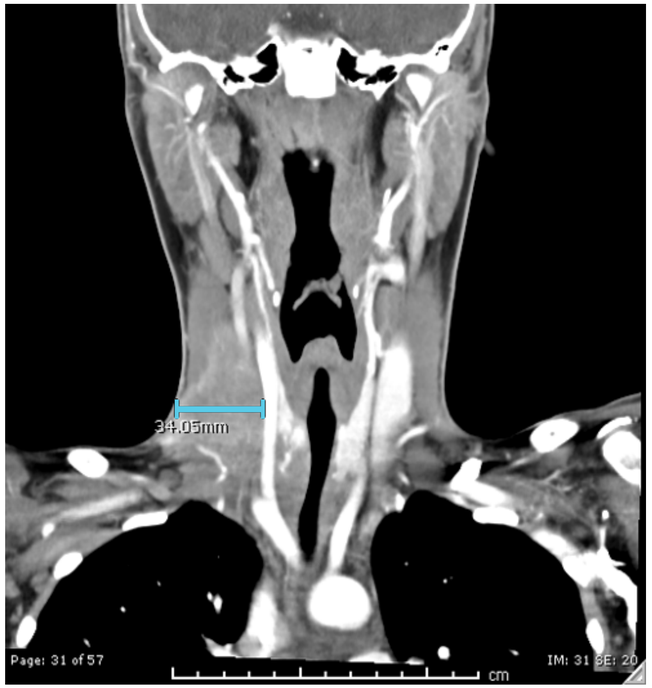


A cycle is 28 days

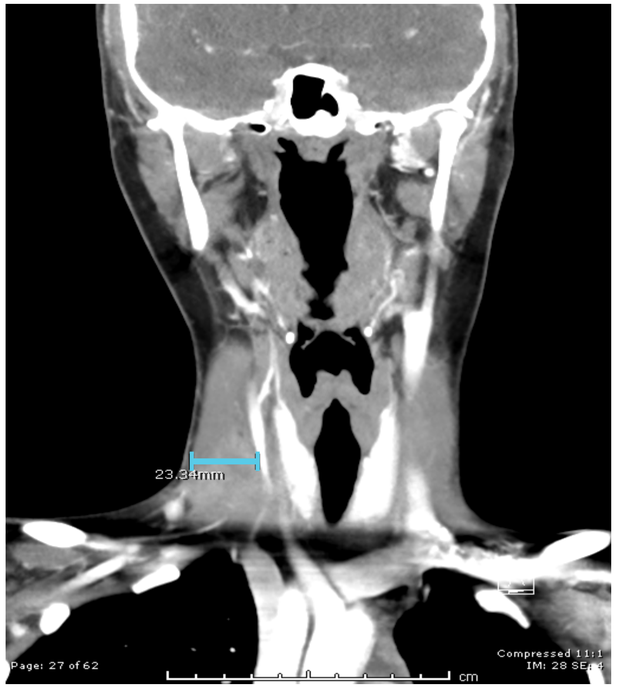
Case Study: 15-year-old with MTC

- **Diagnosis:**
  - *RET L790F* mutant MTC diagnosed 2019
- **Prior therapy:**
  - No prior therapies
- **Selpercatinib started 2020**
  - Reached PR (investigator assessed) at 7.3 months of treatment, treatment ongoing at 14.7 months
  - Also achieved recannulation of the right internal jugular vein
  - No related AEs

Pre-Selpercatinib: Baseline



On-Selpercatinib: Cycle 16



A cycle is 28 days

Conclusions

- **Selpercatinib can be safely administered in pediatric patients at adult equivalent exposures. Overall safety profile is consistent with adult experience.**
- **These data provide further evidence that selpercatinib is effective in pediatric patients in *RET* mutant MTC and *RET* fusion-positive thyroid cancer. These patients should be universally screened for *RET* alterations.**
- ***RET* alterations in pediatric cancers beyond MTC and thyroid cancer are rare.**
    - As expected, no responses were observed for RET variants of unknown significance
- **LIBRETTO-121 study (NCT03899792) is still enrolling patients with *RET*-altered solid or primary CNS tumors.**
    - Phase 1: patients ≤2 years old
    - Phase 2: patients >2 years old at RP2D of 92mg/m^2 BID

Scan or click the QR code or use this URL (https://lillyscience.lilly.com/congress/AmOncMtgJun2021) for a list of all Lilly content presented at the congress

Acknowledgements

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Enrollment is Ongoing

Australia
Sydney Children's Hospital
Royal Children's Hospital Melbourne

Canada
The Hospital for Sick Children

Denmark
Rigshospitalet

France
Gustave Roussy

Germany
Universitätsklinikum Heidelberg

Italy
Fondazione IRCCS Istituto Nazionale dei Tumori

Japan
National Cancer Center Hospital

Korea
Seoul National University Hospital

Spain
Hospital Universitari Vall d'Hebron

United States
Children's Hospital Los Angeles
Lucile Packard Children's Hospital
Children's Hospital Colorado
Dana Farber Cancer Institute
University of Minnesota Hospital
Memorial Sloan Kettering Cancer Center
Cincinnati Children's Hospital Medical Center
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