HSD30

Real-world REarranged during Transfection [RET]-alteration testing, treatment and referral patterns of patients with medullary and papillary thyroid cancer [MTC, PTC] in Taiwan

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BACKGROUND

- Patients with RET mutation-positive MTC have poorer prognosis at 10 year follow up; however, the prognostic impact of RET fusion in patients with PTC remains unclear[1,2].
- Genetic testing for RET mutations or fusions is recommended to individualize therapy for advanced or metastatic medullary or differentiated thyroid cancer respectively[3]
- Selective RET inhibitors are recommended in the treatment of RET mutation-positive advanced or metastatic MTC and RET fusion-positive advanced or metastatic differentiated thyroid cancer, including PTC[3].
- Limited information is available on RET-testing in Taiwan.

OBJECTIVES

The objectives of this study were to descriptively analyse:

- Referral patterns of patients with MTC or PTC at initial diagnosis, advanced disease diagnosis and initiation of systemic drug treatment.
- The proportion of patients with MTC or PTC who undergo biomarker testing for RET, including the methods used.
- Results of biomarker testing for actionable RET alterations among MTC and PTC patients.
- Barriers to RET testing amongst physicians who treat MTC or PTC.
- Surgeries underwent by patient to treat locally advanced disease.
- First line systemic drug treatment patterns for patients with MTC or PTC.

STUDY DESIGN

Step 1
30 physicians in Taiwan were recruited during H2 2020 to complete the Disease Specific Program™ (DSP)

Step 2
Each physician completed an attitudinal survey assessing workload and behaviour

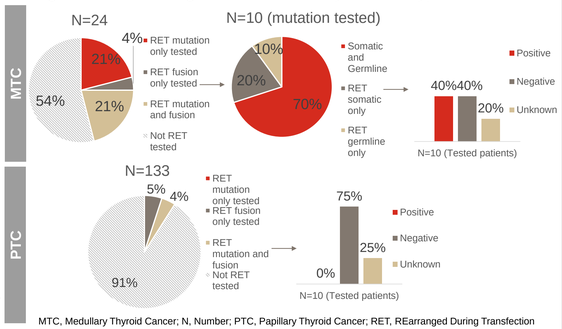
Step 3
Each physician completed a patient record form (PRF) for the next four Consulting patients with MTC or PTC

- Real world data were drawn from the Adelphi Thyroid Cancer DSP, a point-in-time survey conducted from July-December 2020
- Physicians abstracted data from patients' electronic medical records to complete the PRFs.
- Participating patients were ≥18 years old and had a physician confirmed diagnosis of MTC or PTC.

RET TESTING RATES AND RESULTS

- 46% and 9% of MTC and PTC patients underwent biomarker testing for RET respectively (Figure 3).
- 25% and 4% of MTC and PTC patients respectively received a test for a non-targetable RET alteration (Figure 3).
- 40% of MTC patients tested for RET mutation were RET mutation-positive, whilst no PTC patients tested for RET fusion were RET fusion-positive (Figure 3).

Figure 3. RET testing and test results by disease type



MTC, Medullary Thyroid Cancer; N, Number; PTC, Papillary Thyroid Cancer; RET, REarranged During Transfection

CONCLUSIONS

- Less than 50% and 10% of patients with MTC and PTC respectively in this sample underwent a biomarker test for RET.
- Testing barriers amongst physicians were similar for MTC and PTC, with the most common being high cost of testing and lack of reimbursement. Other barriers included inaccessibility, poor proximity and lack of education
- A proportion of MTC and PTC patients received tests for RET fusions and mutations respectively, which are not targetable in the respective tumour types, further indicating a warrant for improved education on targetable RET alterations by tumour type.
- With the recent approval of RET selective treatments in thyroid cancer, further analysis of treatment patterns is required to understand the impact of RET alteration status on treatment selection and outcomes.

Physician and Patient Characteristics

Table 1. Physician characteristics

	Physicians (N=30)
Physician primary specialty, N (%)	
Hematologist/ Medical oncologists	18 (60)
Endocrinologist/Diabetologist	12 (40)
Practice in Private hospitals, N (%)	17 (57)
Practice in Comprehensive Cancer Centre, N (%)	8 (27)
Practice in Public hospital, N (%)	6 (20)
Practice in Private office, N (%)	2 (7)
Median number of patients by tumour type seen by physician (IQR)[µ]	
MTC	1 (1-3)
PTC	13 (5-33)

IQR, Interquartile Range; MTC, Medullary Thyroid Cancer; N, number; PTC, Papillary Thyroid Cancer; [µ] At data capture

Table 2. Patient demographics and clinical characteristics by disease type

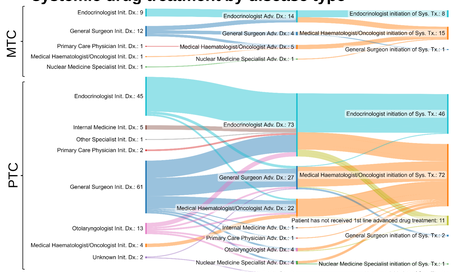
	MTC (N=24)	PTC (N=133)
Median age (IQR) [†, µ]	55 (45-65)	58 (50-69)
Female, N (%)	18 (75)	92 (69)
ECOG 0-1, N (%)[ª]	23 (96)	127 (95)
Median time since diagnosis (IQR) [†,ª]	4 (2-6)	5 (3-9)
Disease stage, N (%)[µ]		
Locally advanced	8 (33)	31 (23)
Metastatic disease	16 (67)	100 (75)

ECOG, Eastern Cooperative Oncology Group; IQR, Interquartile Range; MTC, Medullary Thyroid Cancer; N, number; PTC, Papillary Thyroid Cancer
[†] Reported in years, [ª]At initial thyroid cancer diagnosis, [µ] At data capture, [ª]Captured for patients with a known date of diagnosis

Referral Patterns

- The initial diagnosis was done most commonly by a general surgeon (MTC, 50%; PTC, 46%), advanced diagnosis by an endocrinologist (MTC, 58%; PTC, 55%), and systemic treatment was typically initiated by a medical hematologist / oncologist (MTC, 62%; PTC, 59%) (Figure 1).

Figure 1. Referral pathway of patients at initial diagnosis, advanced diagnosis and initiation of systemic drug treatment by disease type

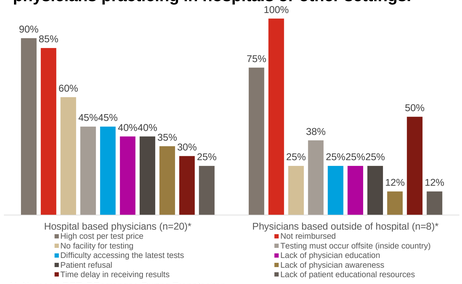


Adv. Dx., Advanced Diagnosis; Init Dx, Initial Diagnosis; MTC, Medullary Thyroid Cancer; PTC, Papillary Thyroid Cancer; Sys. Tx., Systemic Treatment

Barriers to Testing

- The most common barrier to testing for RET alteration in both physicians treating MTC and PTC was a lack of reimbursement (MTC, 82%; PTC, 80%), followed by high cost per test (MTC,79%; PTC, 80%).
- Barriers to RET testing amongst physicians practicing inside or outside of hospitals are summarized in figure 2.

Figure 2. Top 10 Barriers to testing for RET amongst physicians practicing in hospitals or other settings.



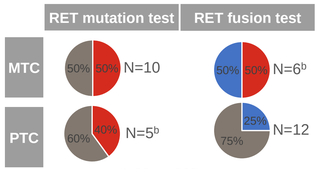
N, Number; RET, REarranged During Transfection

*Hospital includes public and private hospitals without practicing in other areas, whilst other areas include comprehensive cancer centers, public and private offices without practicing in hospitals

RET Testing methods, Timings and Turnaround Time

- RET mutation testing was performed by NGS and PCR in roughly equal proportions, whilst RET fusion testing was performed by NGS, PCR and FISH (Figure 4).

Figure 4. Methods used to test for RET by disease type



FISH; Flourescence in situ hybridization; MTC, Medullary Thyroid Cancer; PCR, Polymerase Chain Reaction; PTC, N, number; NGS, Next Generation Sequencing; Papillary Thyroid Cancer; RET, REarranged During Transfection
[b]Patients tested for a non-targetable RET alteration

RET Testing Timings

- Of patients who had known dates for undergoing a RET test and for advanced disease diagnosis (N=6 for MTC and N=6 for PTC), 67% MTC patients and 83% of PTC patients received a RET test after advanced diagnosis.

RET Testing Turnaround Time

- For patients who had known dates for undergoing a RET test and receiving results, (N= 7 MTC, N=12 PTC), median time to receive results of the latest test was 14 (IQR: 14-14) days for MTC patients and 14 (IQR: 14-26) days for PTC patients.

Surgery and First Line Treatment

- 50% of MTC and 61% of PTC patients underwent surgery for advanced disease (Figure 5a).
- 42% of MTC patients and 43% of PTC patients received first-line (1L) drug treatment (Figure 5b).

Figure 5a. Surgery underwent at advanced disease by disease type

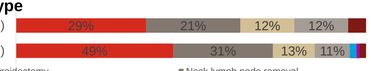
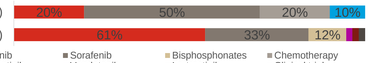


Figure 5b. First line drug treatment received by disease type



Bisphosphonates contains Zoledronic acid and Pamidronate; Chemotherapy contains Cisplatin and 5FU; MTC, Medullary Thyroid Cancer; PTC, Papillary Thyroid Cancer; Values <5% are not reported

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1. Filetti, S., Durante, C., Hartl, D., Leboulleux, S., Locati, L.D., Newbold, K., Papotti, M.G. and Berruti, A. (2019). Thyroid cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology, 30(12), pp.1856–1883.
2. Liu, Y., Wu, S., Zhou, L., Guo, Y. and Zeng, X. (2020). Pitfalls in RET Fusion Detection Using Break-Apart FISH Probes in Papillary Thyroid Carcinoma. The Journal of Clinical Endocrinology & Metabolism, 106(4), pp.e1129–e1138.
3. Filetti, S., Durante, C., Hartl, D.M., Leboulleux, S., Locati, L.D., Newbold, K., Papotti, M.G. and Berruti, A. (2022). ESMO Clinical Practice Guideline update on the use of systemic therapy in advanced thyroid cancer. Annals of Oncology, 33(7), pp.674–684. doi:https://doi.org/10.1016/j.annonc.2022.04.009.

Disclosures: Grace Segall, Audrey Chang, Alice Wei, Urpo Kiiskinen and Min-Hua Jen are employees and shareholders of Eli Lilly and Company. Isaac Sanderson, Katie Lewis and Alex Rider are employees of Adelphi Real World and have no conflicts of interest.

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