

甲状腺髓样癌患者治疗又添新希望——塞尔帕替尼可以有效治疗晚期甲状腺髓样癌

甲状腺髓样癌是甲状腺癌中恶性程度相对较高的甲状腺恶性肿瘤。甲状腺髓样癌来源于滤泡旁降钙素分泌细胞，也称 C 细胞。这种细胞排列成巢状或囊状，并且无乳头或滤泡结构，呈未分化状，其恶性程度介于甲状腺乳头状癌与甲状腺未分化癌之间。晚期转移性甲状腺髓样癌的治疗以靶向治疗为主，目前我国已经批准上市的靶向药物有：安罗替尼以及普拉提尼。上述两种药物的临床研究均由我院牵头，证实了在中国人群中可以有效缓解晚期甲状腺髓样癌患者的肿瘤病灶。

天津市抗癌协会甲状腺癌专业委员会前任主委、天津医科大学肿瘤医院高明教授团队在肿瘤学 2 区杂志《Therapeutic advances in Medical Oncology》(IF:5.48) 又发表最新论文，高明教授牵头的全国多中心 II 期临床试验证实，塞尔帕替尼可以有效缩小晚期甲状腺髓样癌患者靶病灶，降低降钙素及 CEA 水平，为我国晚期甲状腺髓样癌患者的治疗策略增添重要的科学依据。

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THERAPEUTIC ADVANCES in
Medical Oncology

Original Research

Efficacy and safety of selpercatinib in Chinese patients with advanced *RET*-altered thyroid cancers: results from the phase II LIBRETTO-321 study

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研究发现，塞尔帕替尼在晚期甲状腺髓样癌患者中的总体疾病控制率（DCR）为：65.5%，其中最佳疗效为部分缓解（PR）的患者达到 48.3%，疾病稳定状态（SD）患者比例为：35.3%；令人兴奋的是，有 1 例患者在服用塞尔帕替尼后达到了完全缓解（CR），即肿瘤完全消失不见。总体客观缓解率达到：58.6%。

Table 2. Antitumor activity of selpercatinib by IRC in patients with *RET*-mutant MTC.

	PAS MTC*			All MTC [‡]		
	Total (n=26)	Pre-treat d (n=9)	Treatment-naïv (n=17)	Total (n=29)	Pre-treated (n=12)	Treatment-naïve (n=17)
ORR, % [95% CI] ^{‡,§}	57.7* [36.9–76.6]	55.6 [21.2–86.3]	58.8 [32.9–81.6]	58.6 [38.9–76.5]	58.3 [27.7–84.8]	58.8 [32.9–81.6]
Best response, %						
CR	2 (7.7)	1 (11.1)	1 (5.9)	3 (10.3)	2 (16.7)	1 (5.9)
PR	13 (50) [†]	4 (44.4)	9 (52.9)	14 (48.3) [†]	5 (41.7)	9 (52.9)
SD	10 (38.5)	4 (44.4)	6 (35.3)	11 (37.9)	5 (41.7)	6 (35.3)
Progressive disease	0	0	0	0	0	0
Not evaluable	1 (3.8)	0	1 (5.9)	1 (3.4)	0	1 (5.9)
% [95% CI] [§] (CR/PR/SD persisting for ≥16 weeks)	61.5 [40.6–79.8]	55.6 [21.2–86.3]	64.7 [38.3–85.8]	65.5 [45.7–82.1]	66.7 [34.9–90.1]	64.7 [38.3–85.8]

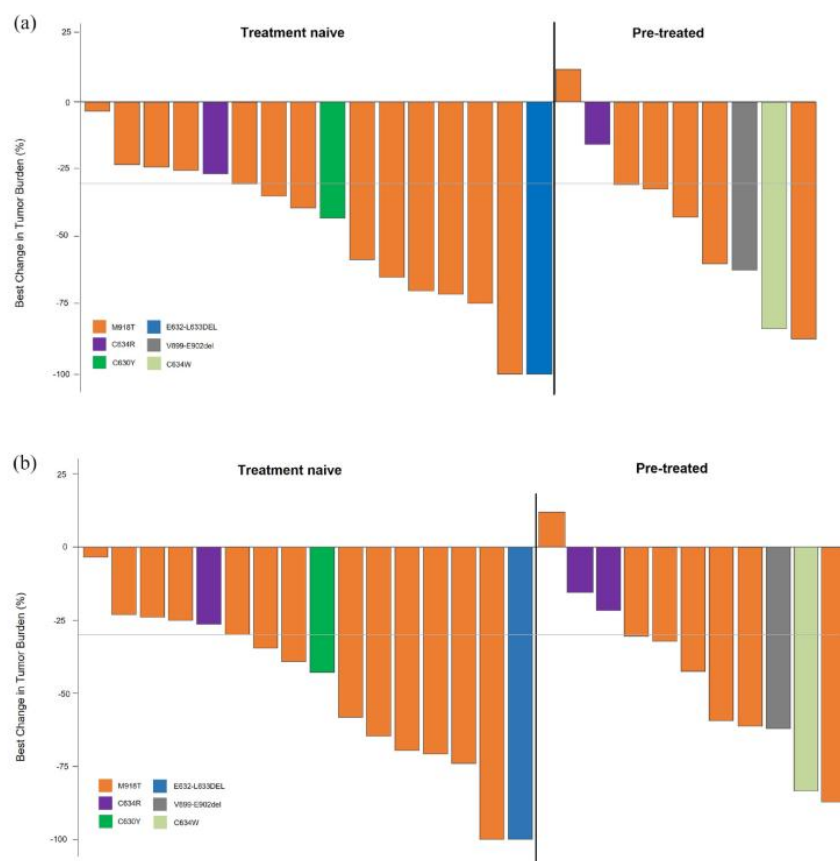
*Patients with *RET*-mutant MTC whose *RET* status was confirmed by central laboratory.

[‡]All enrolled patients with *RET*-mutant MTC.

[†]Not including three patients who achieved PR pending confirmation.

[§]CI, confidence interval; CR, complete response; IRC, independent review committee, MTC, medullary thyroid cancer; ORR, objective response rate; PAS, primary analysis set; PR, partial response; RET, Rearranged during Transfection; SD, stable disease.

CI, confidence interval; CR, complete response; IRC, independent review committee, MTC, medullary thyroid cancer; ORR, objective response rate; PAS, primary analysis set; PR, partial response; RET, Rearranged during Transfection; SD, stable disease.



另外，塞尔帕替尼在具有抗肿瘤作用的同时，其副作用也较小，患者耐受度较高，与多靶点靶向药物相比，其副作用的发生率以及发生的程度均表现出优势。

Table 3. AEs in all selpercatinib-treated patients (n=77).

AE, n (%)	AEs, regardless of attribution					TRAEs		
	Percent of patients with an event					Grade 3	Grade 4	Any grade
	Grade 1	Grade 2	Grade 3	Grade 4	Any grade			
ALT increased*	30 (39.0)	8 (10.4)	11 (14.3)	1 (1.3)	50 (64.9)	11 (14.3)	1 (1.3)	48 (62.3)
AST increased*	31 (40.3)	4 (5.2)	12 (15.6)	0	47 (61.0)	12 (15.6)	0	47 (61.0)
Blood bilirubin increased	21 (27.3)	9 (11.7)	0	0	30 (39.0)	0	0	30 (39.0)
Thrombocytopenia*	18 (23.4)	4 (5.2)	6 (7.8)	2 (2.6)	30 (39.0)	6 (7.8)	2 (2.6)	29 (37.7)
Hypertension*	2 (2.6)	11 (14.3)	15 (19.5)	0	28 (36.4)	12 (15.6)	0	26 (33.8)
Hypoalbuminemia	18 (23.4)	6 (7.8)	2 (2.6)	0	26 (33.8)	1 (1.3)	0	20 (26.0)
Diarrhea*	21 (27.3)	3 (3.9)	1 (1.3)	0	25 (32.5)	1 (1.3)	0	22 (28.6)
White blood cell count decreased	11 (14.3)	11 (14.3)	3 (3.9)	0	25 (32.5)	3 (3.9)	0	24 (31.2)
Dry mouth*	22 (28.6)	0	0	0	22 (28.6)	0	0	21 (27.3)
Blood alkaline phosphatase increased	14 (18.2)	6 (7.8)	1 (1.3)	0	21 (27.3)	1 (1.3)	0	19 (24.7)
Bilirubin-conjugated increased	13 (16.9)	5 (6.5)	2 (2.6)	0	20 (26.0)	2 (2.6)	0	20 (26.0)
Neutrophil count decreased	7 (9.1)	10 (13.0)	3 (3.9)	0	20 (26.0)	3 (3.9)	0	19 (24.7)
Electrocardiogram QT prolonged*	12 (15.6)	1 (1.3)	6 (7.8)	0	19 (24.7)	5 (6.5)	0	15 (19.5)
Hyperuricemia	19 (24.7)	0	0	0	19 (24.7)	0	0	16 (20.8)
Blood creatinine increased*	11 (14.3)	7 (9.1)	0	0	18 (23.4)	0	0	18 (23.4)
Blood lactate dehydrogenase increased	16 (20.8)	2 (2.6)	0	0	18 (23.4)	0	0	16 (20.8)
Weight increased	7 (9.1)	11 (14.3)	0	0	18 (23.4)	0	0	9 (11.7)
Gamma-glutamyltransferase increased	10 (13.0)	5 (6.5)	2 (2.6)	0	17 (22.1)	2 (2.6)	0	16 (20.8)
Edema*	13 (16.9)	4 (5.2)	0	0	17 (22.1)	0	0	14 (18.2)
Pyrexia*	15 (19.5)	2 (2.6)	0	0	17 (22.1)	0	0	12 (15.6)

AEs categorized and graded according to the National Cancer Institute-Common Terminology Criteria for Adverse Events v5.0.
*Consolidated AE term. AEs listed here are those that occurred at any grade in at least 20% of the patients, regardless of attribution.
AEs, adverse events; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TRAEs, treatment-related AEs.

这项新的研究揭示了塞尔帕替尼具有治疗晚期甲状腺髓样癌患者的强大治疗作用，同时也为国内甲状腺外科医生增添了重要的治疗资料。本研究中天津市人民医院高明教授为文章通讯作者，天津医科大学肿瘤医院郑向前教授为文章的第一作者。

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