

出國報告（出國類別：出席國際會議）

2019 歐洲腫瘤醫學年會(ESMO)
與會心得分享

服務機關：病理檢驗部 分子病理科

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摘要

ESMO (European Society for Medical Oncology)歐洲腫瘤醫學年會為全球指標性的癌症醫學重要會議之一，大會邀請了涵蓋肺癌、乳癌、大腸直腸癌等各種癌症領域的專家、醫師、癌症研究者、腫瘤基礎研究人員，於會議中發表了各癌症的最新進展，目的在提升癌症的整合性治療，如標靶治療、免疫療法。全球知名的各大藥廠也在此會中發表了旗下新開發的藥品與新的治療方法和臨床數據，提供了癌症治療及檢測的新方向。此次有機會可以前往西班牙巴塞隆納參與 2019 ESMO 大會，發表被大會接受的壁報論文，除了可以獲得國際專家意見之外，也可從會議內容獲取新知及最新相關研究，因為癌症的治療日新月異，而國際大型會議上的最新發表正大大的影響癌症的未來進展。

關鍵字：歐洲腫瘤醫學年會

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一、 目的

ESMO 為全球指標性的癌症醫學重要會議之一，今年與會人數為近 30000 人，藉著本次參加 2019 歐洲腫瘤學學會壁報論文發表，除了拓展眼界，汲取新知，此次所發表之論文，未來更預計投稿國際論文期刊，藉此壁報發表機會可獲國際專家之寶貴意見。再者，本分子病理科業務為發展癌症病理診斷及相關之分生檢測，此會議議程包含癌症的治療發展及最新相關研究，將有助本科未來業務之發展，增加醫院競爭力。

二、 過程

本次會議於西班牙巴塞隆納的 Gran Via 會場舉行，搭乘飛機到西班牙巴塞隆納後，需搭乘地鐵到會場。會議為期五天(09/27-10/1)，第一天(09/27)報到後會拿到本次會議所有演講的介紹、詳細的會議議程、筆記本以及補助的五天地鐵票，以及識別證。經由大會給的會議議程、電子牆或是 ESMO App 可以選擇自己有興趣的演講，其餘時間能到廠商區了解生物醫學以及生物科技在產業界的趨勢。第二天(09/28)為海報展示，當天早上 9 點至下午 6 點為展示時間，中午 12 點至下午 1 點為討論時間，討論時間除了和不同的與會人員針對海報內容互相交流想法與討論之外，也去看了其他的研究成果增加新知。第三天至第四天(9/29~30)聆聽腫瘤相關演講，第四至五天(9/30~10/1)結束參訪，返回台灣。

三、 心得及建議

歐洲腫瘤醫學年會 ESMO 與 ASCO(美國臨床腫瘤醫學會)、AACR(美國癌症研究協會)為全球三大癌症醫學大會，今年 ESMO 會議舉辦在西班牙的巴塞隆納，巴塞隆納早在十九世紀就知道國際化的重要，從 1988 年的萬國博覽會開始，一直積極舉辦國際性的展覽及會議，躍升為主要的國際展會城市之一，對巴塞隆納來說，會議產業剛好和觀光產業互補，在旅遊淡季時，國際會議的舉辦帶給地方許多的經濟效益。

這次的 ESMO 辦在巴塞隆納的 Gran Via 展區，此展區是歐洲最大，最現代化的展覽會場地之一。它的特點是其設計，功能性和對環境的可延續性。會場有 7 個展廳，各展廳內更有許多的會議室可供使用，可容納 3,000 至 12,000 人。展會位置位在地鐵及機場線附近，交通十分便利，前往展區時，沿途前往 ESMO 的人潮成為最方便的導航，我只要跟著人潮走，就能抵達 ESMO 會場，可見 ESMO 的規模之大。展區劃分成會議室、廠商攤位及海報展示區，會議室依議程不同大小也有不同，最大可容納 2000 人，若會議室座位已滿，在會議室外有提供螢幕及耳機可同步收看，在展會期間，除了海報的展示之外，也前往聆聽幾場演講，「Practical use of liquid biopsy for advanced NSCLC」、「Next immunotherapy strategies for lung cancer」、「ctDNA vs tissue biopsy」、「Optimal delivery of immuno-oncology in advanced NSCLC」等演講，場場座無虛席。其中「ctDNA vs tissue biopsy」這場演講是在探討 liquid biopsy 及 tissue biopsy 的優缺點，這場演講利用電子投票系統，以 Q&A 的方式即時統計出與會人士的意見，

在兩方辯論之後再統計一次，所有的提問並無標準答案，最後再請專家解釋演講前後統計數據改變的可能原因，提供了新的思考方向，這真是有趣的體驗。

廠商攤位區也是讓人目不暇給，除了進駐了全球各大知名藥廠，發表最新治療方向及藥物，今年最大亮點仍是免疫療法，每個攤位為了吸引大家的目光，以動畫或投影的方法介紹各家藥廠的最新發現，有助於癌症患者的治療。

海報展示區展示了各領域對癌症研究的結果，依照癌症種類劃分展示區域，我們的論文展示在「NSCLC, metastatic」海報區，這是我第一次在國際會議展示海報，覺得十分緊張，在海報討論及意見交流的時間，面對提問，我盡我所能的回答，雖然無法回答得很好，但是提問者都會給予微笑並稱讚，讓我的神經不那麼緊繃，也能更有自信的面對提問。在展示海報時我發現，歐美人士對於自己的海報展示是相當有自信的，面對提問也往往是以意見交流的方式討論；相對於我在展示海報時和面對提問時的緊張，態度上有明顯的差別，提問並不等於是我們的研究有做不好的地方，而是提問者感到有興趣，應更有自信的回答才是。

這次投稿海報論文能獲ESMO大會接受，要感謝分子病理科團隊的大力幫助，及主任們的鼓勵與支持；也十分感謝臺北榮總提供參加國際學術會議的機會，讓我可以拓展視野及對未來學術研究的動力有所助益。

四、附錄

本次壁報論文題目

Disease monitoring of EGFR mutation-positive NSCLC patients via circulating tumor DNA

Disease monitoring of EGFR mutation-positive NSCLC patients via circulating tumor DNA

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BACKGROUND

Activating mutations within the tyrosine kinase domain of the epidermal growth factor receptor (EGFR) are present in lung adenocarcinomas ranging from 10%-14% in Caucasian to 40%-50% in Asian populations [1-3]. The most common alterations include exon 19 deletions and the L858R point mutation in exon 21. The presence of these mutations is associated with sensitivity to EGFR tyrosine kinase inhibitors (TKIs), although patients achieve great benefit from anti-EGFR therapies, unfortunately, all patients eventually develop resistance to the treatment and have disease progression.

Liquid biopsy is a non-invasive way to obtain samples for molecular profiling. Easy sampling provides the opportunity for frequent disease monitoring and ability to assess disease-specific genomic alterations in real time. The cobas® EGFR Mutation Test v2 has the capability to detect and follow patients with EGFR sensitizing mutations to evaluate longitudinal changes in EGFR mutation status during TKI treatment; it also can detect T790M, a resistant mutation to first and second generation TKIs. The assay also offers a unique tool called Semi-Quantitative Index (SQI), which is a measure of the amount of mutant ctDNA in a sample that can be used to monitor/track/measure the evolution of EGFR mutations over time.

In this study, we hypothesized that monitoring EGFR mutations during TKI treatment could indicate response to therapy earlier and predict for progressive disease (PD), and we also examined whether early detection of T790M or an increasing level of the original sensitizing EGFR mutation could be a sign of therapy resistance.

METHODS

Two hundred thirty-two NSCLC patients from a single clinical site in Taiwan were enrolled in this study. This analysis is focused on those patients who were EGFR mutation positive by cobas® EGFR Mutation Test v2 assay. Plasma samples were tested with the cobas® EGFR Mutation Test v2, and the SQI values for each mutation were reported by the software for the target mutation. The SQI is used to reflect a trend in the plasma EGFR mutation level. Molecular progression (MP) is defined as 1.5 increase in SQI values or detection of T790M.

Patient clinical responses to TKI therapy was assessed by RECIST 1.1. Molecular response was defined as no detection of EGFR mutations in plasma sample by cobas® EGFR Mutation Test v2. Cumulative incidence method was used to estimate the time to both clinical and molecular response. Time to clinical progression and molecular progression were estimated using Kaplan-Meier method, and stratified Cox proportional hazards model was used to assess the association of each category.

Figure 1. Flow diagram of patients included in the study

RESULTS

Table 1. Demographics and Baseline Clinical Characteristics

Characteristic	Overall	CR	MR	MP	Clinical Progression
Demographics					
Age (years)	62.7 (10.1)	62.5 (10.2)	62.8 (10.0)	62.9 (10.1)	62.7 (10.1)
Gender					
Male	155 (50.3%)	43 (54.5%)	43 (54.5%)	43 (54.5%)	43 (54.5%)
Female	151 (48.7%)	35 (45.5%)	35 (45.5%)	35 (45.5%)	35 (45.5%)
Stage					
Advanced	137 (43.5%)	33 (42.3%)	33 (42.3%)	33 (42.3%)	33 (42.3%)
Metastatic	172 (54.1%)	40 (51.6%)	40 (51.6%)	40 (51.6%)	40 (51.6%)
Baseline Clinical Characteristics					
First Line Treatment					
TKI	185 (58.1%)	47 (60.3%)	47 (60.3%)	47 (60.3%)	47 (60.3%)
Chemotherapy	133 (41.9%)	31 (39.7%)	31 (39.7%)	31 (39.7%)	31 (39.7%)
TKI + Chemotherapy	21 (6.6%)	5 (6.4%)	5 (6.4%)	5 (6.4%)	5 (6.4%)
Time to event (months)					
To clinical progression	38.1 (12.5)	43.0 (13.8)	43.0 (13.8)	43.0 (13.8)	43.0 (13.8)
To molecular progression	15.5 (11.5)	15.5 (11.5)	15.5 (11.5)	15.5 (11.5)	15.5 (11.5)
To both clinical and molecular progression	17.2 (13.2)	17.2 (13.2)	17.2 (13.2)	17.2 (13.2)	17.2 (13.2)
Time to event (months) (95% CI)					
To clinical progression	38.1 (34.5-41.7)	43.0 (39.3-46.7)	43.0 (39.3-46.7)	43.0 (39.3-46.7)	43.0 (39.3-46.7)
To molecular progression	15.5 (14.0-17.0)	15.5 (14.0-17.0)	15.5 (14.0-17.0)	15.5 (14.0-17.0)	15.5 (14.0-17.0)
To both clinical and molecular progression	17.2 (15.7-18.7)	17.2 (15.7-18.7)	17.2 (15.7-18.7)	17.2 (15.7-18.7)	17.2 (15.7-18.7)

The most common EGFR mutations detected in the tissue were L858R (54%) and Exon 19 deletion (Ei569del) (46%). One patient had both Ex19del and T790M mutations. And there was one patient with both Ex19del and Ex20ins. Almost identical prevalence was observed in the plasma EGFR mutation positive population.

Table 2. Agreement between plasma and tissue mutation results at baseline

	Tissue Mutation Positive	Plasma Mutation Positive	Total
Tissue Mutation Positive	221	201	422
Tissue Mutation Negative	11	47	58
Total	232	248	480
Agreement (%)	94.8%	84.7%	94.8%
Disagreement (%)	5.2%	15.3%	5.2%
Kaplan-Meier P-value	0.0001	0.0001	0.0001

For this analysis we have examined 106-patient baseline samples (of the 231 screened patients) that were tested with both cobas® EGFR Mutation Test v2 tissue and plasma assays. The positive agreement between tissue and plasma EGFR variant detection is 74.2%, which is in line with others reported.

Figure 2. Time to response – molecular vs. clinical

To explore the relationship between clinical response (CR and PR based on RECIST 1.1) and molecular response. Cumulative incidence approach was used to look at the subset of patients from the 101 patient population who had a clinical response (73 patients) and a molecular response (94 patients). As shown in Figure 2, molecular responses can predict clinical responses.

Figure 3. Time to progression – molecular vs. clinical

Analysis of the serial plasma collected from patients who progressed while on 1st line TKI showed re-appearance of the original EGFR sensitizing mutations with increasing SQI levels or appearance of a T790M mutation. T790M mutation was detected in 28% (24/101) of the patients on TKI treatment. We have estimated the time to progression differences (molecular progression vs. clinical progression) using Kaplan-Meier method. The median time difference between molecular progression and clinical progression is 3.1 months with a log-rank p value of 0.008.

Figure 4. Bar chart of time to clinical vs. molecular progression

CONCLUSIONS

This study clearly demonstrated that monitoring EGFR mutation levels or mutation changes in blood could be a meaningful approach to predict clinical progression for lung adenocarcinoma patients treated with EGFR TKI.

Using cobas® EGFR Mutation Test v2, detection of molecular response or progression was 1.6 and 3.1 months prior to clinical response or progression, respectively.

Early detection of disease progression may provide additional information and time for physicians to identify optimal next line therapy.

It warrants further studies to demonstrate potential utility, such as early intervention, of serial blood EGFR testing in NSCLC management.

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Table 3. Clinical and molecular progression status for patients with both clinical and molecular responses

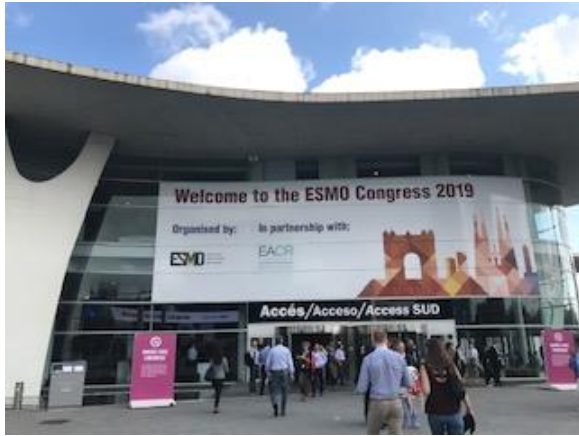
Molecular Progression	Clinical Progression (Yes)	Clinical Progression (No)	Total
Yes	42	14	56
No	3	10	13
Total	45	24	69

Table 4. Median and mean time to progression for patients with both molecular and clinical progression

	N	Median	Mean
Time to Clinical Progression	42	10.1	11.5
Time to Molecular Progression	42	6.5	7.9

Table 5. Time to progression – molecular vs. clinical

Category	N	Median (months)	Mean (months)
Molecular Progression	42	6.5	7.9
Clinical Progression	42	10.1	11.5



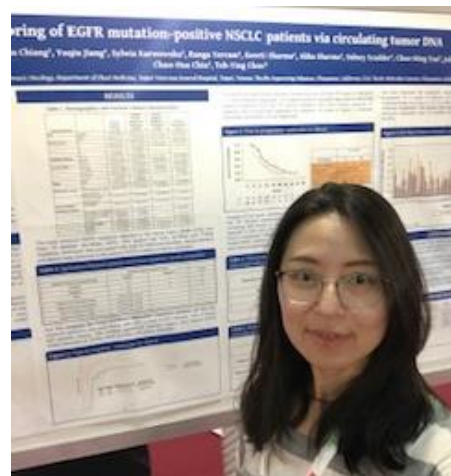
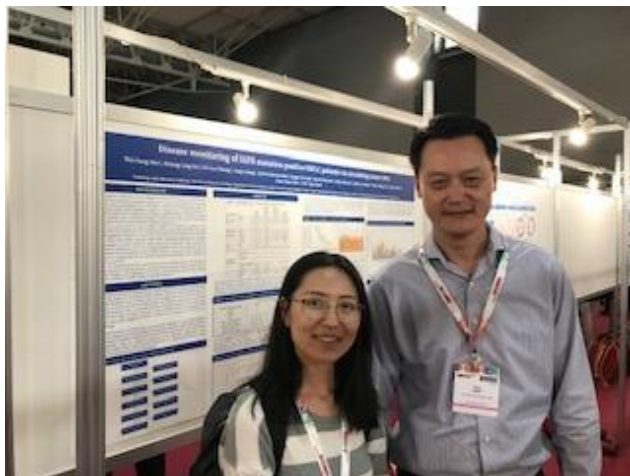
Gran Via 展區



報到處



會議室



海報展示

返國知識分享：2019/10/16

