癌症檢測健保給付與產業發展

陳淑貞博士

行動基因 技術長

全民健康保險醫療服務給付項目及支付標準共同擬訂會議

108年第一次

會議資料

EGFR基因檢測支付規範相關規定

(二) 新增「肺癌表皮生長因子受體(EGFR)突變體外診斷醫療器材檢測(In Vitro Diagnostics, IVD)與肺癌表皮生長因子受體(EGFR)突變實驗室自行研發檢測(Laboratory Developed Test, LDT)等2項分子病理檢測」，詳表一序號2（附件2，頁次討1-13）：

1. 依108年第2次專家諮詢會議結論，同意新增EGFR基因檢測惟僅支付IVD檢測方法，支付規範相關規定如下：

(1) 建議適應症範圍：

A. 限復發或轉移性(第IV期)之非小細胞且非鱗狀上皮肺癌，於使用EGFR標靶藥物前得申請檢測。

B. 第IIIB期及第IIIC期，經肺癌多專科團隊討論，無法以外科手術完全切除、且不適合放射化學治療，於使用EGFR標靶藥物前得申請檢測。

(2) 建議支付規範：

A. 限使用已確診之腫瘤病理組織或細胞檢體做檢測，並於檢測報告上註明診斷與腫瘤體積百分比。

B. 限具肺癌EGFR基因檢測項目通過CAP(美國病理學家學會，The College of American Pathologists)、TAF(財團法人全國認證基金會，Taiwan Accreditation Foundation)或台灣病理學會之分子實驗室認證之實驗室以醫療院所為單位進行申報。

C. 限使用食品藥物管理署核准之第三等級醫療器材檢測試劑操作，並於檢測報告上註明方法學與檢測平台。

D. 限解剖病理專科醫師簽發報告，並於檢測報告上加註專科醫師證書字號。

E. 限符合適應症規範下用藥前之伴隨式檢測每人終生限申報1次。

EGFR基因檢測財務評估

財務評估：

經本署校正後建議支付點數為8,252點（附件4，頁次討1-16），預估增加點數92.52百萬點，惟經107年11月12日召開「肺癌EGFR標靶藥物用藥前所需之基因檢測納入健保醫療給付會議」3家藥廠同意一次性調降TKI藥費節省4,532萬元，爰預估增加支出為47.20百萬點。

108 年度第 1 次「全民健康保險醫療服務給付項目及支付標準專家諮詢會議」會議紀錄

壹、 時間：108 年 1 月 16 日上午 9 點 30 分

貳、 地點：台北市信義路 3 段 140 號 9 樓第一會議室

參、 主席：蔡副署長淑鈴　　紀錄：黃思瑄

肆、 出席專家：

李教授炫昇	周副院長輝政
蔡醫師森田	李副院長宏昌
洪主任芳明	吳科主任玉琮
曾教授崴元	
中華民國骨科醫學會	張嘉獻
中華民國血液病學會	林建廷、黃泰中
台灣臨床腫瘤醫學會	賴泓誌

伍、 請假專家：

陳醫師誠仁	郭院長宗正
張醫師效煌	李主任玉雲
莊院長銀清	陳院長振文
吳醫師文正	吳院長美環
台灣消化系醫學會	

陸、 列席單位及人員：

社團法人先天性成骨不全症關懷協會	程健智、林榆芬
臺灣病理學會	賴瓊如、郭冠廷、杭仁釩
國立臺灣大學醫學院附設醫院	鄭文誠
衛生福利部食品藥物管理署	呂在綸、林瑞祥
彰化基督教醫療財團法人彰化基督教醫院	蕭玉鑫
財團法人醫藥品查驗中心	朱素貞
本署醫審及藥材組	黃育文、裴倩倩
本署醫務管理組	谷祖棣、王玲玲、鍾欣穎、陳依婕、林美惠、沈瑞玲、鄧家佩、簡詩蓉、楊瑜真

三、臺灣病理學會建議新增「肺癌表皮生長因子受體(EGFR)突變體外診斷醫療器材檢測(In Vitro Diagnostics, IVD)」與「肺癌表皮生長因子受體(EGFR)突變實驗室自行研發檢測(Laboratory Developed Test, LDT)」等 2 項分子病理檢測案。

討論重點：

(一) 與會專家表示鑑於 LDT 檢測方法現行法規尚未完備，且避免其他檢測項目效仿本項目以 LDT 法檢測造成品質疑慮，建議本案僅支付 IVD 檢測方法，並重申未來藥廠不再補助檢測費用，醫院亦不可向民眾收取自費。

(二) 針對 IVD 檢測方法，建議如下：

1. 依據現行健保規定，執行本項目之院所及受託代檢單位必須為本保險特約醫事服務機構，爰醫院委託代檢予生技產業實驗室部分暫保留，俟相關法規完備後再行研議。

附件 2

表一、108 年建議新增醫療服務給付項目及財務影響評估彙整表(計 2 項目)

序號	中文名稱	主要臨床功能及目的	替代項目及替代率				預算推估				實際淨增加點數(百萬點) I=①G ②G-H	
			名稱	表定支付點數 C	替代率 D	點數差值 E=A-C	預估全國執行量 F=B	預估年增點數(百萬點) G= ①A*F*(1-D) +E*F*D ②A*F		一次性調降 TKI 藥費所節省費用 H		
1	經皮移除心臟內電極導線	為避免過多的心臟內電極導線滯留在血管內，造成大靜脈阻塞、感染、心臟瓣膜閉鎖不全、干擾心節律器功能等不良後果，以經皮及靜脈使用特材的方式移除心臟內舊有損壞或無功能的電極導線。	管心物術留處小>)	30,356	20%	6,607	50	1.54	①		1.54	①
2	肺癌表皮生長因子受體(EGFR)突變檢測	表皮生長因子受體突變分析(EGFR mutation)為晚期非小細胞肺癌患者使用標靶藥物「表皮生長因子受體抑制劑的伴隨檢測(companion testing)」，若檢測結果為陽性，方可使用此類標靶藥物治療。					11,212	92.52	②	45.32	47.20	②
											48.75	

表皮生長因子受體突變分析(EGFR mutation)為晚期非小細胞肺癌患者使用標靶藥物「表皮生長因子受體抑制劑的伴隨檢測(companion testing)」，若檢測結果為陽性，方可使用此類標靶藥物治療。

附件 5

全民健康保險醫療服務給付項目及支付標準

第二部 西醫

第二章 特定診療 Specific Diagnosisand Treatment

第一節 檢查 Laboratory Examination

第二十四項 伴隨式診斷 Companion Diagnostics (30101~30200)

編號	診療項目	基層院所	地區醫院	區域醫院	醫學中心	支付點數
30101B	肺癌表皮生長因子受體(EGFR)突變 EGFR mutation in lung cancer 註： 1.適應症： (1)限復發或轉移性(第IV期)之非小細胞且非鱗狀上皮肺癌，於使用EGFR標靶藥物前得申請檢測。 (2)第IIIB期及第IIIC期，經肺癌多專科團隊討論，無法以外科手術完全切除、且不適合放射化學治療，於使用EGFR標靶藥物前得申請檢測。 2.支付規範： (1)限使用已確診之腫瘤病理組織或細胞檢體做檢測，並於檢測報告上註明診斷與腫瘤體積百分比。 (2)限具肺癌EGFR基因檢測項目通過CAP(美國病理學家學會，The College of American Pathologists)、TAF(財團法人全國認證基金會，Taiwan Accreditation Foundation)或台灣病理學會之分子實驗室認證之實驗室以醫療院所為單位進行申報。 (3)限使用食品藥物管理署核准之第三等級醫療器材檢測試劑操作，並於檢測報告上註明方法學與檢測平台。 (4)限解剖病理專科醫師簽發報告，並於檢測報告上加註專科醫師證書字號。 (5)限符合適應症規範下用藥前之伴隨式檢測每人終生限申報1次。		v	v	v	8252

Approved EGFR IVD in Taiwan

許可證字號	分類分級	中/英文品名	申請商
衛部醫器製字第004963號	Class III B4020分析特定試劑	台塑生醫EGFR基因突變檢測套組 Formosa EGFR Mutation Detection Kit	台塑生醫科技股份有限公司
衛部醫器輸字第028935號	Class III B4020分析特定試劑	羅氏EGFR基因突變檢驗套組第二代 cobas EGFR Mutation Test v2	台灣羅氏醫療診斷設備股份有限公司
衛部醫器輸字第025535號	Class III B1860免疫病理組織化學試劑與套組	“凱杰” 表皮生長因子接受器擴增反應突變檢驗試劑組 "QIAGEN” therascreen EGFR RGQ PCR kit	凱杰生物科技有限公司
衛部醫器輸字第030485號	Class III B4020分析特定試劑	“凱杰” 表皮生長因子接受器擴增反應突變檢驗試劑組 “QIAGEN” therascreen EGFR RGQ PCR kit	凱杰生物科技有限公司
衛部醫器陸輸字第000668號	Class III B1860免疫病理組織化學試劑與套組	“麗寶生醫” 人類EGFR基因突變檢測試劑盒(螢光PCR法) AmoyDx EGFR 29 Mutations Detection Kit	麗寶生命醫學股份有限公司

三、臺灣病理學會建議新增「肺癌表皮生長因子受體(EGFR)突變體外診斷醫療器材檢測(In Vitro Diagnostics, IVD)」與「肺癌表皮生長因子受體(EGFR)突變實驗室自行研發檢測(Laboratory Developed Test, LDT)」等 2 項分子病理檢測案。

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Journal of Personalized Medicine

MDPI

J. Pers. Med. (2017) 7, 5; doi:10.3390/jpm7030005

Article

The Clinical and Economic Impact of Inaccurate EGFR Mutation Tests in the Treatment of Metastatic Non-Small Cell Lung Cancer

Mindy M. Cheng [1,*], John F. Palma [2], Sidney Scudder [1], Nick Poulios [1] and Oliver Liesenfeld [1]

1 Roche Molecular Systems, Inc., 4300 Hacienda Dr., Pleasanton, CA 94588, USA; sid.scudder@roche.com (S.S.); nick.poulios@roche.com (N.P.); oliver.liesenfeld@roche.com (O.L.)

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* Correspondence: mindy.cheng@roche.com; Tel.: +1-925-251-6705

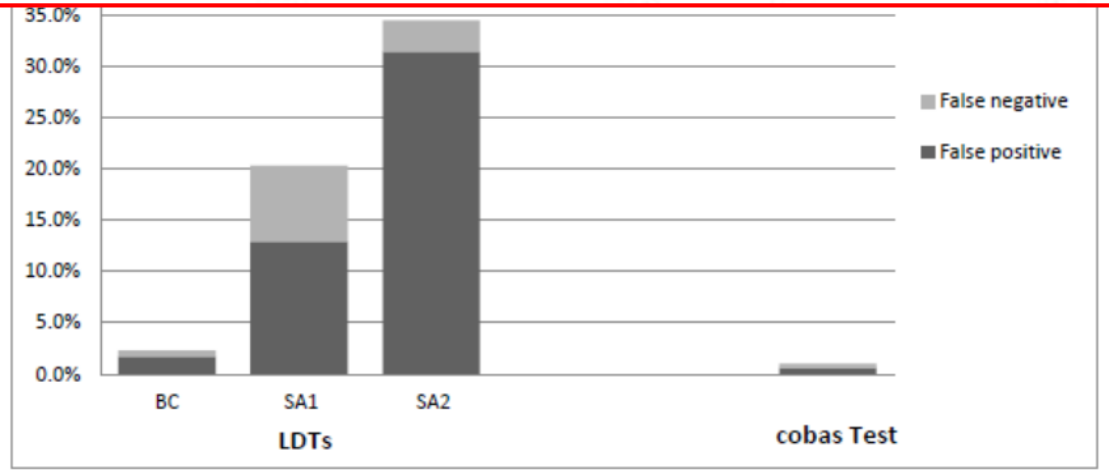

Figure 2. Individual Patient Probability of Misclassification by LDTs and the cobas Test. LDTs = Laboratory-developed tests; BC = Base-case; SA = Scenario analysis.

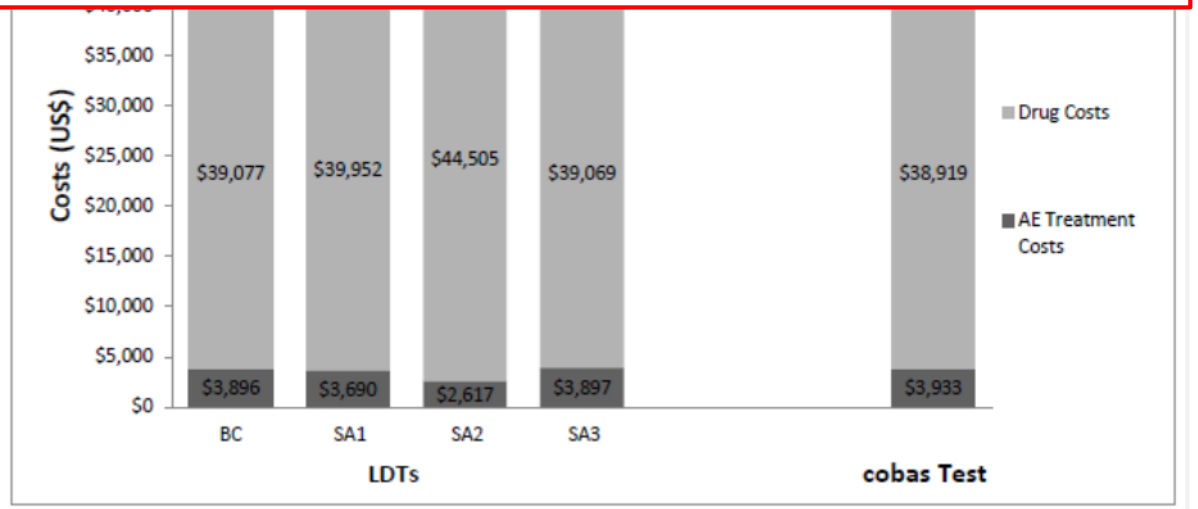

Figure 3. Difference in treatment costs per tested patient between LDTs and the cobas Test.

JAMA Oncology (2018) 4:838-841

JAMA Oncology | Brief Report

Comparison of Laboratory-Developed Tests and FDA-Approved Assays for *BRAF*, *EGFR*, and *KRAS* Testing

Annette S. Kim, MD, PhD; Angela N. Bartley, MD; Julia A. Bridge, MD; Suzanne Kamel-Reid, PhD; Alexander J. Lazar, MD, PhD; Neal I. Lindeman, MD; Thomas A. Long, MPH; Jason D. Merker, MD, PhD; Alex J. Rai, PhD; David L. Rimm, MD, PhD; Paul G. Rothberg, PhD; Patricia Vasalos, BA; Joel T. Moncur, MD, PhD

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6 College of American Pathologists, Northfield, Illinois.
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9 Yale University School of Medicine, New Haven, Connecticut.
10 Strong Memorial Hospital, University of Rochester Medical Center, Rochester, New York.
11 Walter Reed National Military Medical Center, Bethesda, Maryland.

IMPORTANCE The debate about the role of the Food and Drug Administration (FDA) in the regulation of laboratory-developed tests (LDTs) has focused attention on the analytical performance of all clinical laboratory testing. This study provides data comparing the performance of LDTs and FDA-approved companion diagnostics (FDA-CDs) in proficiency testing (PT) provided by the College of American Pathologists Molecular Oncology Committee.

DESIGN, SETTING, AND PARTICIPANTS This comparison of PT responses examines the performance of laboratories participating in the College of American Pathologists PT for 3 oncology analytes for which both FDA-CDs and LDTs are used: *BRAF*, *EGFR*, and *KRAS*. A total of 6897 PT responses were included: *BRAF* (n = 2524; 14 PT samples), *EGFR* (n = 2216; 11 PT samples), and *KRAS* (n = 2157, 10 PT samples). US Food and Drug Administration companion diagnostics and LDTs are compared for both accuracy and preanalytic practices of the laboratories.

RESULTS From analysis of 6897 PT responses, this study demonstrates that both LDTs and FDA-CDs have excellent performance overall, with both test types exceeding 97% accuracy for all 3 genes (*BRAF*, *EGFR*, and *KRAS*) combined. Rare variant-specific differences did not consistently favor LDTs or FDA-CDs. Additionally, more than 60% of participants using an FDA-CD reported adapting their assay from the approved procedure to allow for a greater breadth of sample types, minimum tumor content, and instrumentation, changing the classification of their assay from FDA-CD to LDT.

No difference in assay performance between FDA-CDs and LDT

Key Points

Question Are there performance differences between laboratory-developed tests (LDTs) and US Food and Drug Administration–approved companion diagnostics (FDA-CDs [also known as in vitro diagnostics])?

Findings In 6897 proficiency testing responses, both LDTs and FDA-CDs exceed 97% accuracy combined across all comparable molecular oncology proficiency testing samples. In addition, more than 60% of participants using FDA-CDs report modifying the approved procedure to broaden clinical practice, rendering them LDTs.

Meaning This study supports the accuracy and comparable performance of LDTs and FDA-CDs and indicates that the majority of laboratories purchasing in vitro diagnostics for FDA-CDs are in fact using them as LDTs.

Conclusions

We find no differences overall between FDA-CDs and LDTs in assay performance for these 3 analytes, with an average of over 97% accuracy from both types of assays more than the 3 surveys, although a technical limitation of one FDA-CD is noted. This study identified alterations from the FDA-approved procedure in greater than 60% of respondents using FDA-CDs, likely to allow for more clinical practice flexibility. Given the overall comparable performance of FDA-CDs and LDTs, as well as the significant off-label use of FDA-CDs, these data question the distinction between FDA-CDs and LDTs from a regulatory standpoint and note the greater clinically relevant applications of LDTs.

三、臺灣病理學會建議新增「肺癌表皮生長因子受體(EGFR)突變體外診斷醫療器材檢測(In Vitro Diagnostics, IVD)」與「肺癌表皮生長因子受體(EGFR)突變實驗室自行研發檢測(Laboratory Developed Test, LDT)」等 2 項分子病理檢測案。

討論重點：

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Approved EGFR IVD in USA

PMA	Device	Applicant
P030044	EGFR Pharmdx	DAKO NORTH AMERICA, INC.
P120019	Cobas Egfr Mutation Test And Cobas EGFR Mutation Test V2	ROCHE
P120022	Therascreen EGFR Rgq Pcr Kit	QIAGEN MANCHESTER LTD
P150044	Cobas EGFR Mutation Test V2	Roche Molecular Systems, Inc.
P150047	Cobas EGFR Mutation Test V2	Roche Molecular Systems, Inc.

Most Clinical Service Lab in US uses LDTs for their clinical service

Quest Diagnostics™

Lung Cancer Mutation Panel (EGFR, KRAS, ALK)

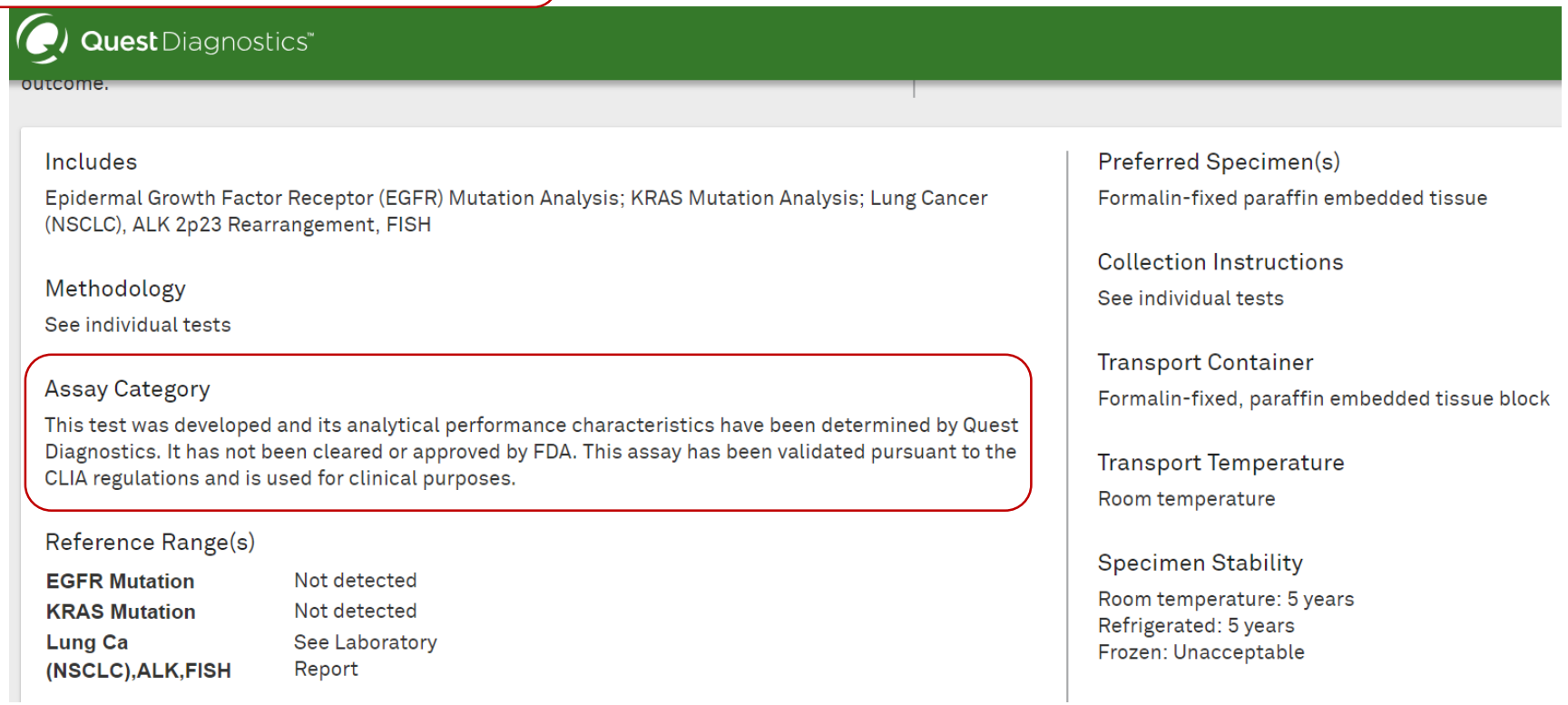
Test Code

91216

CPT Code(s)*

81235**, 81275**, 81276**, 88271** (x2), 88274**

CPT Code is subject to a **MEDICARE LIMITED COVERAGE POLICY and may require a signed ABN when ordering.



https://testdirectory.questdiagnostics.com/test/test-detail/91216/lung-cancer-mutation-panel-egfr-kras-alk?q=EGFR&cc=MASTER

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- Hematology
  - Hematopathology
- Immunology
- Medical Informatics
- Microbiology
- Molecular Diagnostics
- Specimen Procurement
- Transfusion Medicine
- Virology

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Genetics and Solid Tumor Diagnostic Testing

The clinical laboratory offers DNA-based testing for a variety of disorders. For further information on testing, please consult the following links:

- ALK Fusion FISH
- Alpha-Thalassemia
- Alpha-Hemoglobin DNA Sequence
- Beta-Hemoglobin DNA Sequence
- BRAF Mutations
- BROCA – Cancer Risk Panel
- BROCA or EpiPlex™ – Single Gene Testing
- BROCA, ColoSeq™, Epiplex™ – Known Familial Mutation
- ColoSeq™ – Lynch and PolyPosis Panel
- ColoSeq™ Tumor Panel NEW
- ColoSeq™ – Polyposis Panel
- Cystic Fibrosis
- DNA Storage Prior to Testing
- EGFR Mutations

NEW

UW-OncoPlex™ Cancer Gene Panel Featured at SCCA & UW Medicine Precision Medicine

UW-OncoPlex™ is a multiplexed gene sequencing panel that detects mutations in tumor tissue in 262 cancer-related genes for cancer treatment, prognosis, and diagnosis. For more information including how to order and pricing»
Featured at SCCA»
Featured at UW Medicine Precision Medicine»

UW Laboratory Medicine Clinical Test Information

http://depts.washington.edu/labweb/Divisions/MolDiag/MolDiagGen/index.htm

Most University Hospital Service Lab in US also uses LDTs for clinical service

Background on EGFR Mutations

For some lung cancer patients, the mutation status of the EGF receptor gene *(EGFR)* in their tumor tissue is now being predict response to drugs that inhibit the tyrosine-kinase activity of the EGF receptor protein, such as erlotinib and ge

Testing Algorithm

To allow cost-effective testing strategies, two levels of testing are offered:

- **Level 1 (test code EGFRL1)**: The Level 1 test detects the most common somatic mutations in the EGF receptor ge mutations in patients with lung cancer.
- **Level 2 (test code EGFRL2)**: The Level 2 test is usually performed only if the EGFR Mutations Level 1 test is negat mutations account for the remaining ~10% of mutations not detected by the Level 1 test. NOTE: Mutations such testing may be performed without Level 1 when the indication for testing is to assess for resistance mutations.

Requisition Form

UWMC Genetics Requisition

Specimen Requirements and Handling

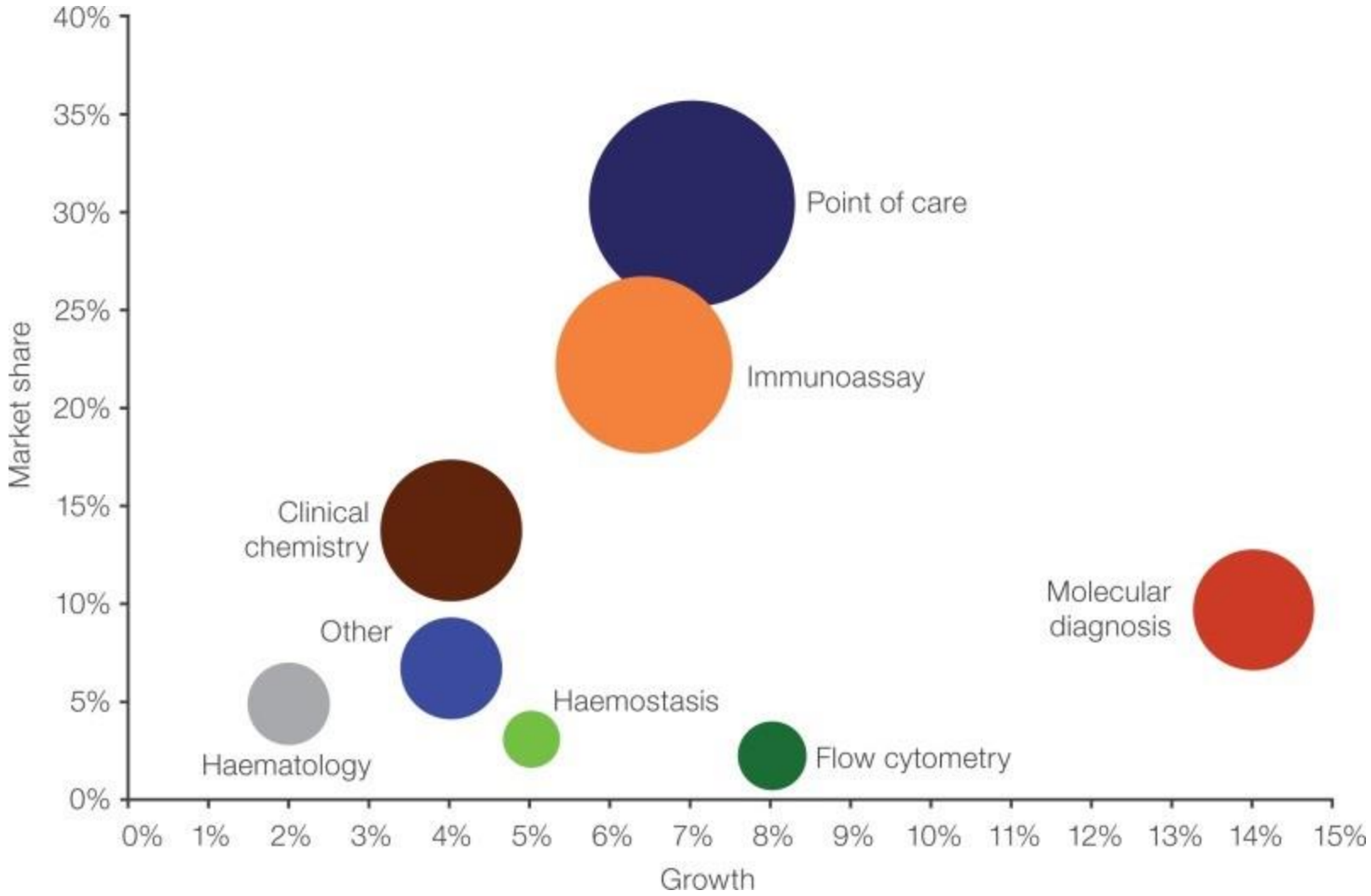
See EGFRL1 or EGFRL2 in the Laboratory Medicine Online Test Guide for details regarding specimen collection, hand

CPT Codes and Pricing

For CPT coding, see the Laboratory Medicine Online Test Guide: Click Here and enter "EGFRL1" or "EGFRL2".

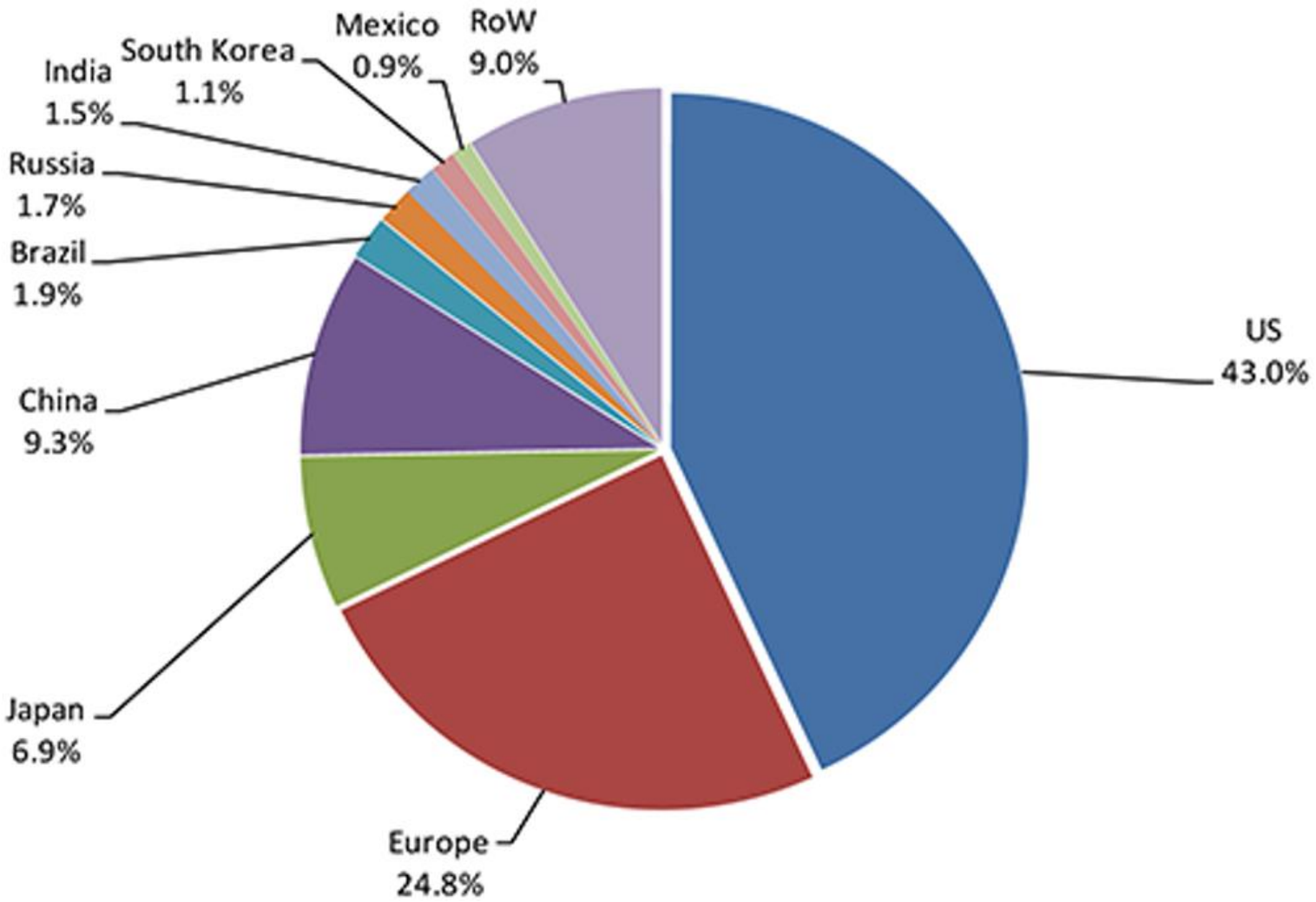
For pricing information, contact Reference Laboratory Services (206)685-6066 or (800)713-5198

Molecular diagnosis is the fastest growing segment in IVD industry

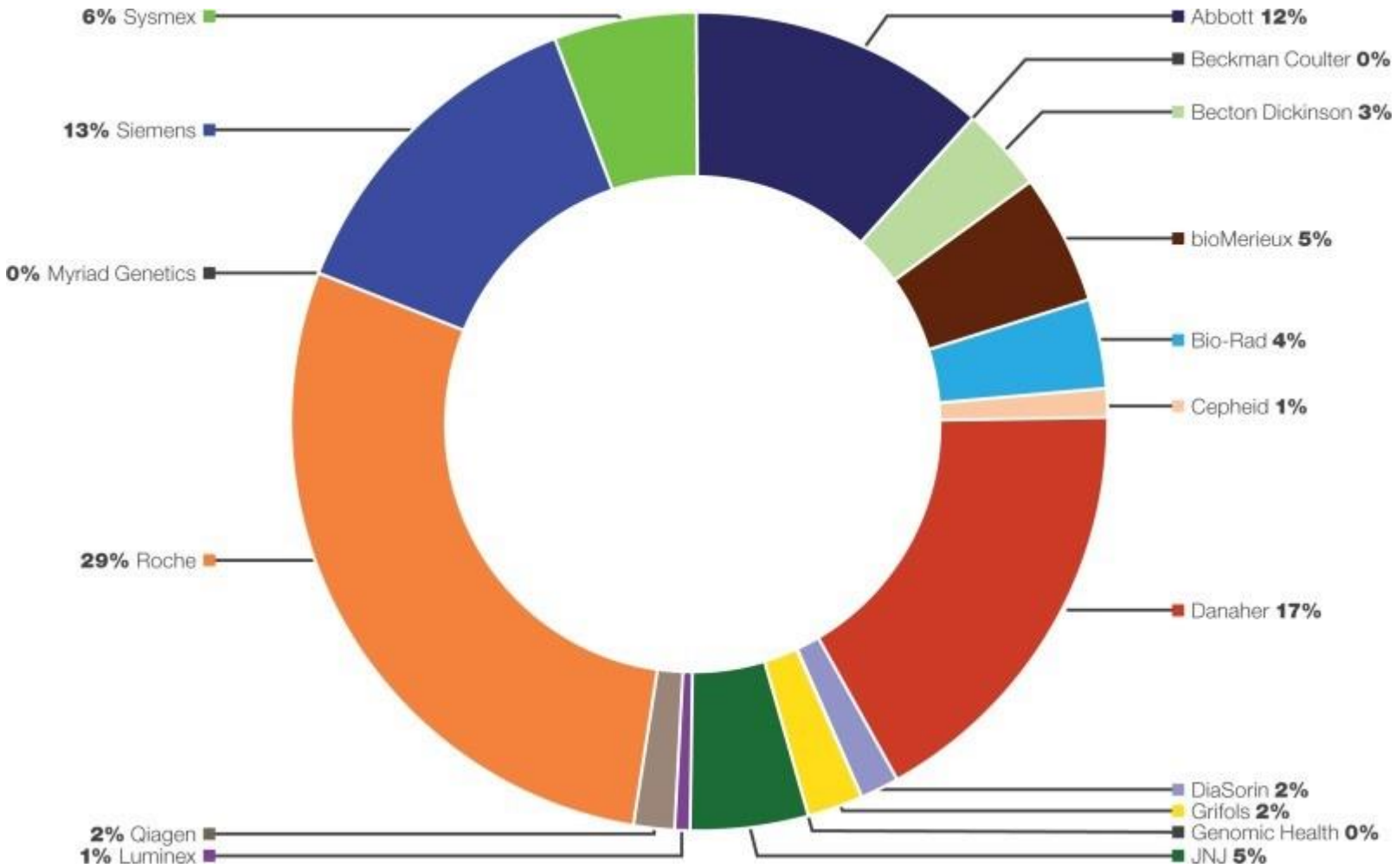


https://investmentbank.com/diagnostics/

Projected 2019 MDx market share by region



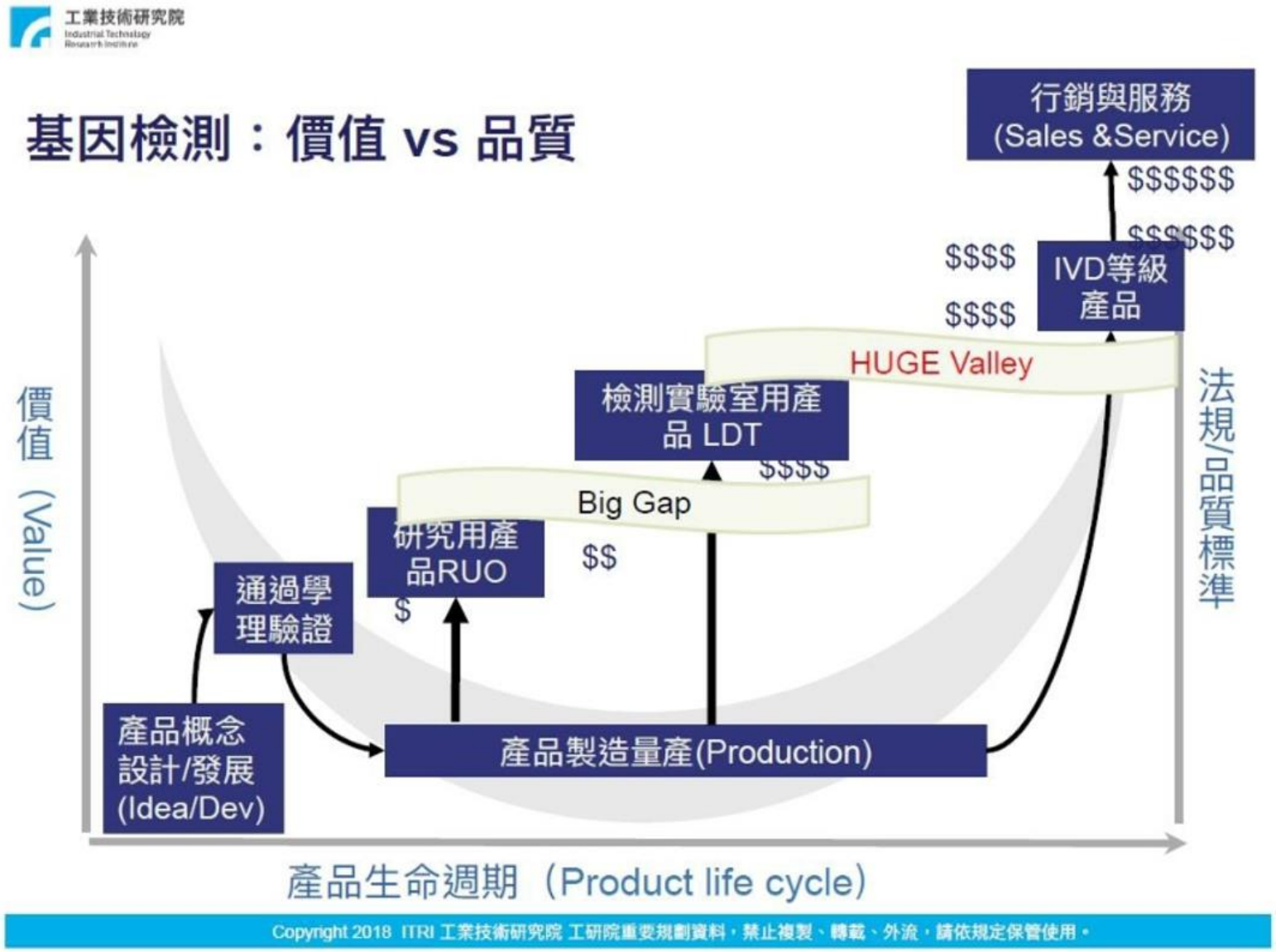
Overall the Global IVD market is dominated by 8-10 key players



Approved EGFR IVD in Taiwan

許可證字號	分類分級	中/英文品名	申請商
衛部醫器製字第004963號	Class III B4020分析特定試劑	台塑生醫EGFR基因突變檢測套組 Formosa EGFR Mutation Detection Kit	台塑生醫科技股份有限公司
衛部醫器輸字第028935號	Class III B4020分析特定試劑	羅氏EGFR基因突變檢驗套組第二代 cobas EGFR Mutation Test v2	台灣羅氏醫療診斷設備股份有限公司
衛部醫器輸字第025535號	Class III B1860免疫病理組織化學試劑與套組	“凱杰” 表皮生長因子接受器擴增反應突變檢驗試劑組 "QIAGEN” therascreen EGFR RGQ PCR kit	凱杰生物科技有限公司
衛部醫器輸字第030485號	Class III B4020分析特定試劑	“凱杰” 表皮生長因子接受器擴增反應突變檢驗試劑組 “QIAGEN” therascreen EGFR RGQ PCR kit	凱杰生物科技有限公司
衛部醫器陸輸字第000668號	Class III B1860免疫病理組織化學試劑與套組	“麗寶生醫” 人類EGFR基因突變檢測試劑盒(螢光PCR法) AmoyDx EGFR 29 Mutations Detection Kit	麗寶生命醫學股份有限公司

LDT is an essential step to the development of IVD



2018/3/22

陳其邁：生技業遭遇困難　行政院會快速解決讓產業有感

1904　出版時間：2019/03/22 20:23

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