

NGS of EGC Patients Treated with ESD

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1. Case presentation

EGC로 ESD받은 환자의 NGS 결과

2. Diagnosis

Early gastric cancer (IIb + IIc)- ADENOCARCINOMA

3. Therapy and Clinical course

ESD로 치료

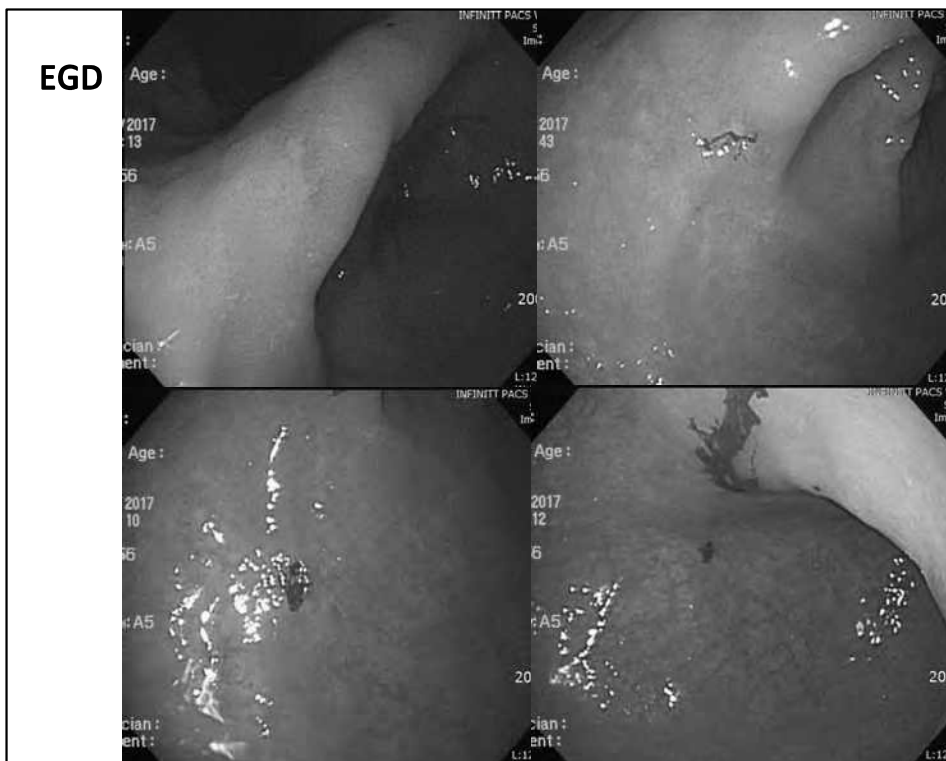
4. Conclusion

NGS의 선별적 보험급여로 인하여 gastric cancer에서도 그 필요성에 대해 논의해 볼 필요가 있으나, 아직 gastric cancer에 대한 target therapy의 효과가 입증되어 있는 약제가 없어 한계가 있겠다.

Key Words: Stomach cancer, NGS

Case 1

- 66 years-old male
- C.C : Detection EGC on screening EGD
- P.I : 개인 내과의원 건진 내시경에서 EGC (AW of angle with adenocarcinoma, moderately moderately differentiated) 진단되어 내원
- P/Ex. Lab : non-specific





Bx.

EARLY GASTRIC CARCINOMA

1. Location : Middle third, Center at Body, lesser curvature
2. Gross type : **EGC type IIb+IIc**
3. Histologic type : **TUBULAR ADENOCARCINOMA, poorly differentiated**
4. Histologic type by Lauren : Intestinal
5. Size : **60 X 34 mm**
6. Depth of invasion : **Invades mucosa (muscularis mucosa) (pT1a)**
7. Resection margin :
 - Lateral : INVOLVEMENT OF CARCINOMA on the angle epicenter side (1 slice)
 - Base : Free from tumor (Safety margin : 0.5 mm)
8. Lymphatic invasion : Not identified
9. Venous invasion : Not identified
10. Perineural invasion : Not identified

NGS

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날짜: 2017. 11. 27 1 / 12

변이 요약

암종류: 위암

이 암 유형에서
 다른 암 유형에서
 이 암 유형과 다른 암 유형에서
 금지됨
 사용 또는 금지
 근거 없음

유전자 변이	US-FDA	US-NCCN	EMA	ESMO	Global Clinical Trials
ERBB2 V777L mutation	✖	○ (2)	✖	✖	● (9)
ERBB2 mutation	✖	○ (2)	✖	✖	● (6)
BAP1 mutation	✖	✖	✖	✖	● (1)

US-FDA: 미국-Food and Drug Administration(식품의약국), **US-NCCN:** 미국-National Comprehensive Cancer Network(국가종합암네트워크), **EMA:** European Medicine Agency(유럽의약국), **ESMO:** European Society for Medical Oncology(유럽종양학회). 괄호 안의 숫자는 증거가 있는 관련 치료법의 수를 나타냅니다.

Final Diagnosis

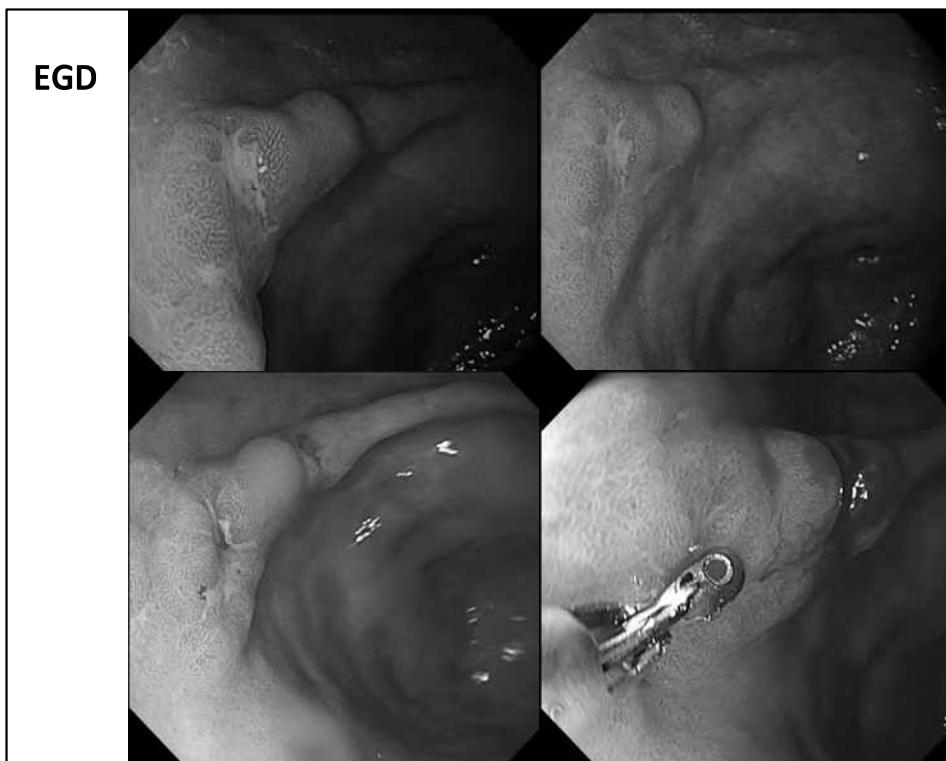
Early gastric cancer (IIb + IIc)

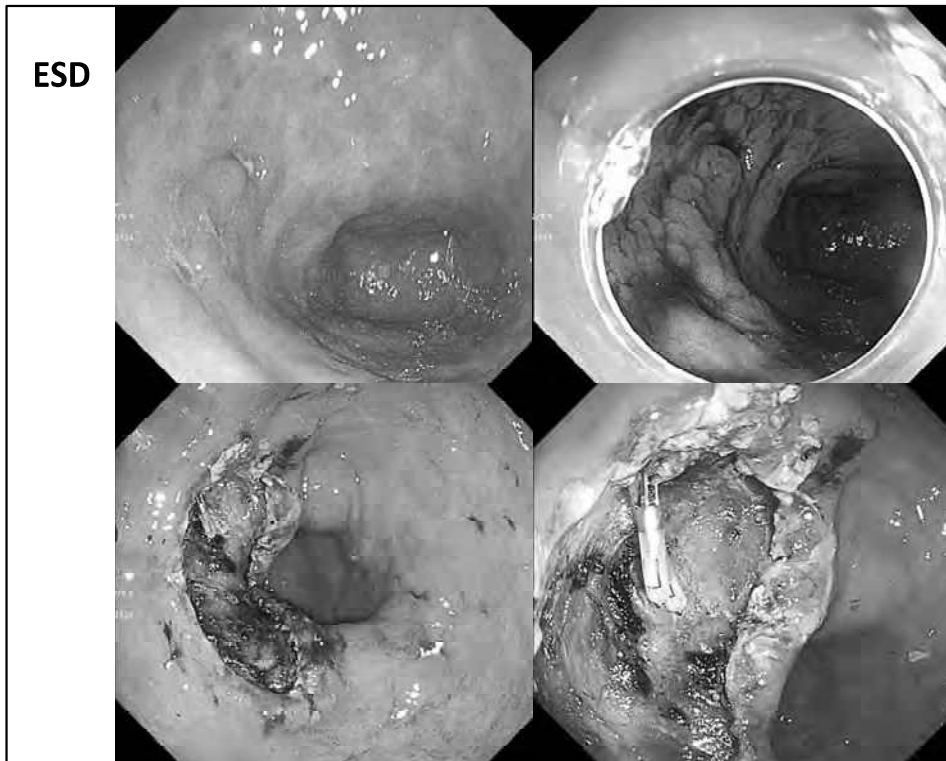
- ADENOCARCINOMA, poorly differentiated

With ERBB2 V777L, ERBB2, BAP1 mutation

Case 2

- 76 years-old male
- C.C : Detection EGC on screening EGD
- P.I : 1개월 전 alcoholic LC 진단받은자로, 검진 내시경에서 EGC의심되어 시행한 bx.에서 adenocarcinoma 확인되어 ESD 위해 입원
- P/Ex. Lab : PLT 138,000, PT INR 1.02, AST/ALT 34/31
T.bil 0.37





Bx.

EARLY GASTRIC CARCINOMA

1. Location : Lower third, Center at Antrum, lesser curvature to anterior wall
2. Gross type : **EGC type IIb+IIc**
3. Histologic type : **TUBULAR ADENOCARCINOMA, moderately differentiated**
4. Histologic type by Lauren : Intestinal
5. Size : **20 X 12 mm**
6. Depth of invasion : **Invades mucosa (muscularis mucosa) (pT1a)**
7. Resection margin :
 - Lateral : Free from tumor (Safety margin : 2 mm, Distal)**
 - Base : Free from tumor (Safety margin : 0.05 mm)**
8. Lymphatic invasion : Not identified
9. Venous invasion : Not identified
10. Perineural invasion : Not identified

NGS

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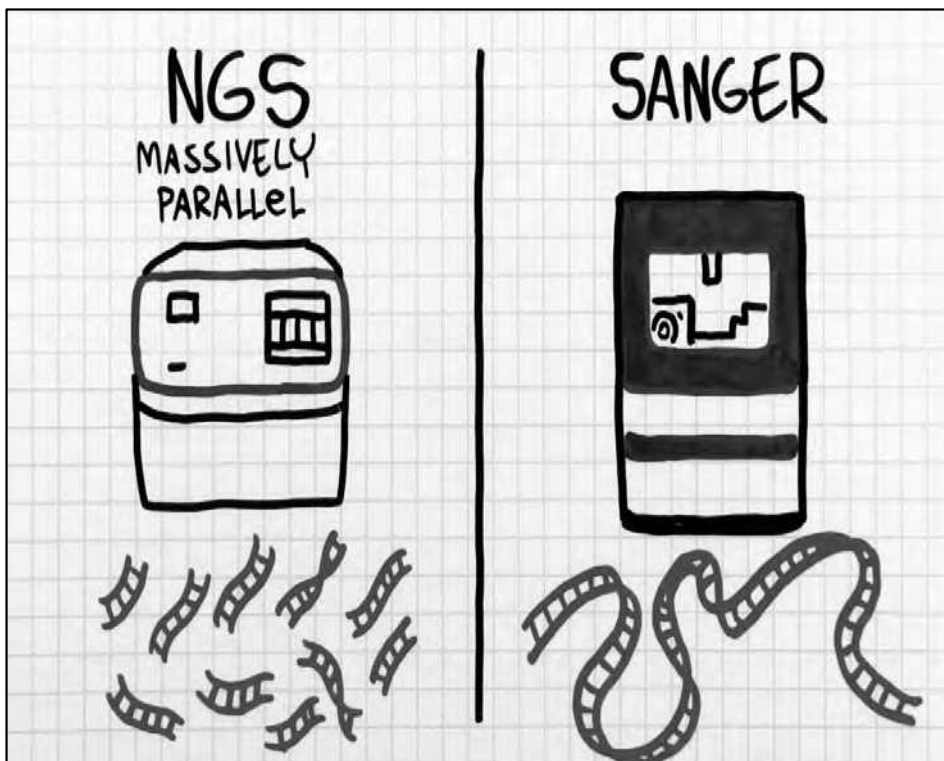
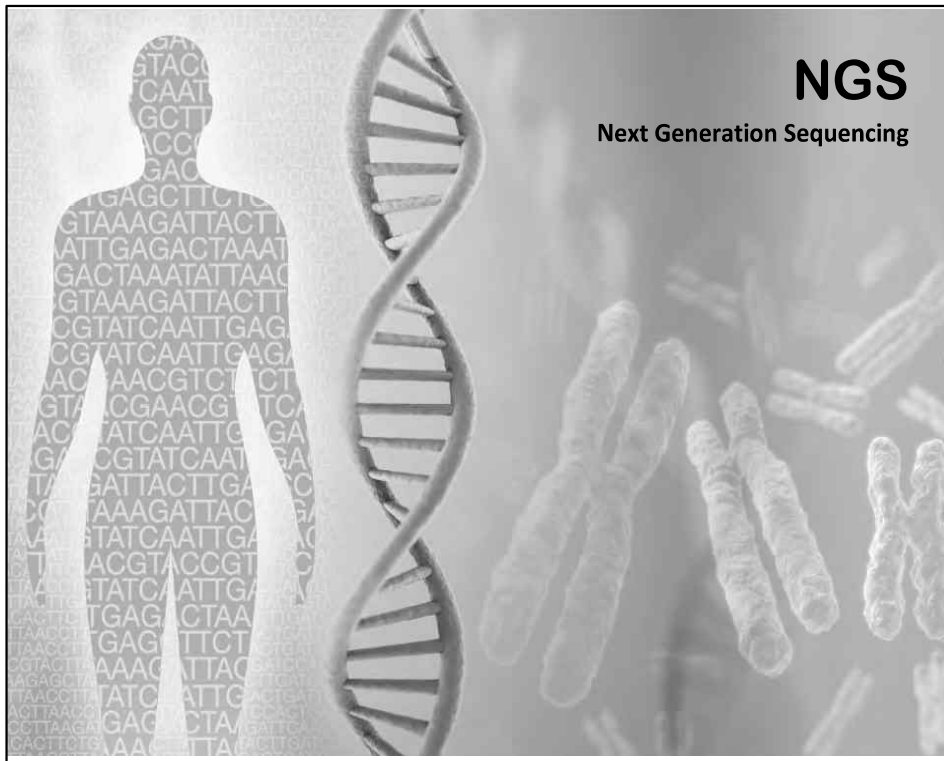
유전자 변이	US-FDA	US-NCCN	EMA	ESMO	Global Clinical Trials
TP53 mutation	✕	✕	✕	✕	● (5)
KRAS amplification	✕	✕	✕	✕	● (7)
FGFR2 amplification	✕	✕	✕	✕	● (12)

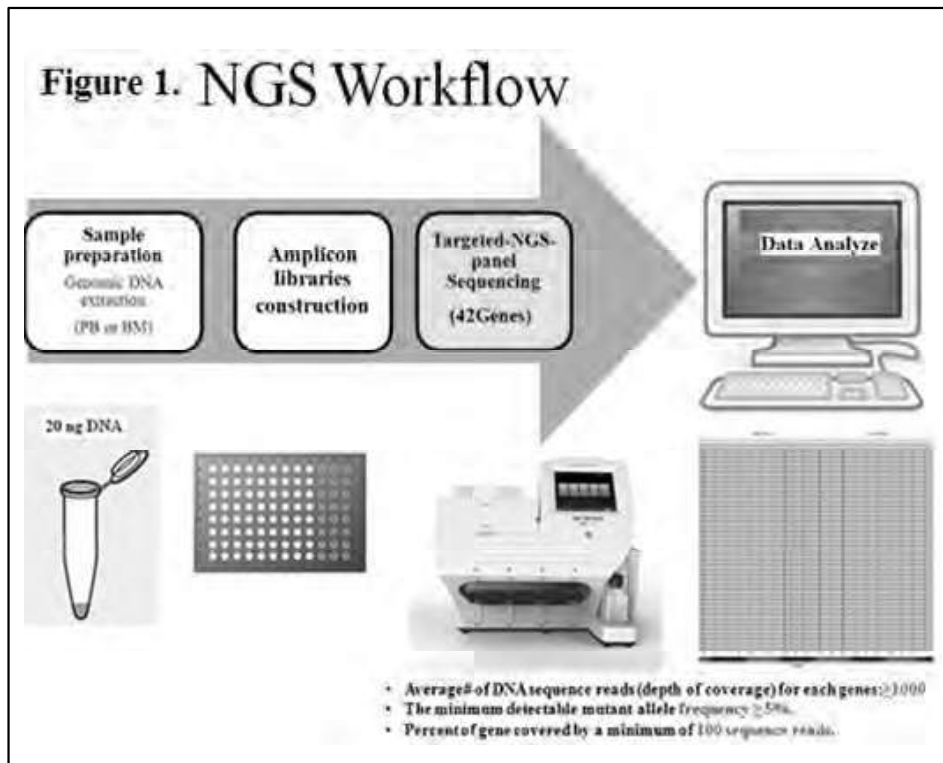
Final Diagnosis

Early gastric cancer (IIb + IIc)

- ADENOCARCINOMA, moderately differentiated

With TP53 mutation, KRAS & FGFR2 amplification





OncoPrint® Comprehensive Panel Gene List

Hotspot genes, n=73 (hotspot coverage)			TSG, n=26 (full gene)	Copy gain, n=49	Fusion drivers, n=22 (183 assays)
ABL1	GNA11	MYD88	APC	ACVRL1	IGF1R
AKT1	GNAQ	NFE2L2	ATM	AKT1	IL6
ALK	GNAS	NPM1	BAP1	APEX1	KIT
AR	HNF1A	NRAS	BRCA1	AR	KRAS
ARAF	HRAS	PAX5	BRCA2	ATP11B	MCL1
BRAF	IDH1	PDGFRA	CDH1	BCL2L1	MDM2
BTK	IDH2	PIK3CA	CDKN2A	BCL9	MDM4
CBL	IFITM1	PPP2R1A	FBXW7	BIRC2	MET
CDK4	IFITM3	PTPN11	GATA3	BIRC3	MYC
CHEK2	JAK1	RAC1	MSH2	CCND1	MYCL
CSF1R	JAK2	RAF1	NF1	CCNE1	MYCN
CTNNB1	JAK3	RET	NF2	CD274(PDL1)	MYO18A
DDR2	KDR	RHEB	NOTCH1	CD44	NKX2-1
DNMT3A	KIT	RHOA	PIK3R1	CDK4	NKX2-8
EGFR	KNSTRN	SF3B1	PTCH1	CDK6	PDCD1LG2
ERBB2	KRAS	SMO	PTEN	CSNK2A1	PDGFRA
ERBB3	MAGOH	SPOF	RB1	DCUN1D1	PIK3CA
ERBB4	MAP2K1	SRC	SMAD4	EGFR	PNP
ESR1	MAP2K2	STAT3	SMARCB1	ERBB2	PPARG
EZH2	MAPK1	U2AF1	STK11	FGFR1	RPS6KB1
FGFR1	MAX	XPO1	TET2	FGFR2	SOX2
FGFR2	MED12		TP53	FGFR3	TERT
FGFR3	MET		TSC1	FGFR4	TIAF1
FLT3	MLH1		TSC2	FLT3	2NF217
FOXL2	MPL		VHL	GAS6	
GATA2	MTOR		WT1		

DNA Panel

Hotspot, CDS, CNV, Fusion, Hotspot + CNV, Hotspot + CNV + Fusion, Hotspot + Fusion, CNV + Fusion

RNA Panel

**NGS 기반 고형암 유전자 패널 검사 보험 수가
(조건부 선별급여, 환자본인부담 50%)**

2017.7.1. 개정 수가

처방명칭 (RNA fusion+질가산포함)	단가(a)	총금액(b)/ 단가(a)*25% (병원가산)	선택진료비(c)/ 단가(a)*30%	본인부담금 (비특진)/ 총금액(b)*50%	본인부담금(특진)/ 총금액(b)*50%+ 선택진료비(c)
NGS 고형암 패널 Level II/ Oncomine Comprehensive 1	1,232,960	1,541,200	369,890	770,600	1,140,490
NGS 고형암 패널 Level I	863,070	1,078,838	258,920	539,420	798,340

(단위: 원)

현재 병리과에서 고형암 패널 level II Oncomine Comprehensive 1 시행 중.
Level I,II custom panel은 추후 시행 예정

CASE 1

Final Diagnosis

Early gastric cancer (IIb + IIc)

- ADENOCARCINOMA, poorly differentiated

With **ERBB2 V777L, ERBB2, BAP1** mutation

ERBB2 V777L mutation					
관련 치료법	US-FDA	US-NCCN	EMA	ESMO	Global Clinical Trials*
afatinib	×	○	×	×	● (II)
trastuzumab	×	○	×	×	×
erlotinib + chemotherapy	×	×	×	×	● (II)
lapatinib	×	×	×	×	● (II)
neratinib	×	×	×	×	● (II)
pertuzumab + trastuzumab	×	×	×	×	● (II)
pirotinib	×	×	×	×	● (I/II)
everolimus + trastuzumab + letrozole	×	×	×	×	● (I)
pyrotinib	×	×	×	×	● (I)
varlitinib + chemotherapy	×	×	×	×	● (I)

ERBB2 mutation					
관련 치료법	US-FDA	US-NCCN	EMA	ESMO	Global Clinical Trials*
afatinib	×	○	×	×	×
trastuzumab	×	○	×	×	×
erlotinib + chemotherapy	×	×	×	×	● (II)
lapatinib	×	×	×	×	● (II)
pirotinib	×	×	×	×	● (I/II)
everolimus + trastuzumab + letrozole	×	×	×	×	● (I)
pyrotinib	×	×	×	×	● (I)
varlitinib + chemotherapy	×	×	×	×	● (I)

BAP1 mutation					
관련 치료법	US-FDA	US-NCCN	EMA	ESMO	Global Clinical Trials*
olaparib	×	×	×	×	● (II)

ERBB2 V777L mutation	
<p>NCT01953926 An Open-label, Multicenter, Multinational, Phase II Study Exploring the Efficacy and Safety of Neratinib Therapy in Patients With Solid Tumors With Activating HER2, HER3 or EGFR Mutations or With EGFR Gene Amplification.</p> <p>암 유형: 위암 변이 등급: ERBB2 activating mutation</p>	<p>다른 식별자: 13-140, 13-615, CTA733, EudraCT Number: 2013-002872-42, IRAS ID: 171670, NCI-2014-00495, PUMA-NER-5201, REec-2014-0843, SUMMIT, SUMMIT basket, TrialTroveID-191740</p> <p>인구 부분: EGFR, Estrogen receptor positive, HER2 positive, Progesterone receptor positive, Second line or greater/Refractory/Relapsed, Stage IV</p> <p>단계: II</p> <p>치료법: neratinib</p> <p>입지: Australia, Finland, Israel, Italy, Republic of Korea, Spain, United Kingdom, United States</p> <p>미국 주: CA, FL, MA, MO, MS, NJ, NY, TN, TX</p> <p>미국 연락처: Puma Biotechnology Clinical Operations [424-248-6500; ClinicalTrials@pumabiotechnology.com]</p>
<p>NCT02091141 My Pathway: An Open Label Phase I/IIa Study Evaluating Trastuzumab/Pertuzumab, Erlotinib, Vemurafenib/Cobimetinib, and Vismodegib in Patients Who Have Advanced Solid Tumors With Mutations or Gene Expression Abnormalities Predictive of Response to One of These Agents</p> <p>암 유형: 위암 변이 등급: ERBB2 activating mutation</p>	<p>다른 식별자: 1403013519, 2014-0459, AAAN9701, J1480, ML28897, ML28897/PRO 02, ML28897PRO/02, My Pathway, NCI-2014-01811, TrialTroveID-205033</p> <p>인구 부분: Second line or greater/Refractory/Relapsed, Stage III, Stage IV</p> <p>제외 기준 변이 등급: ERBB2 amplification, ERBB2 overexpression</p> <p>단계: II</p> <p>치료법: pertuzumab + trastuzumab</p> <p>장소: United States</p> <p>미국 주: AR, AZ, CA, CO, FL, GA, IL, MD, MN, NC, ND, NY, OH, OK, OR, PA, SD, TN, TX, VA, WA</p> <p>미국 연락처: Hoffmann-La Roche, Study Director [888-662-6728; global.roche.genentech.trials@roche.com]</p>

CASE 2

Final Diagnosis

Early gastric cancer (IIb + IIc)

- ADENOCARCINOMA, moderately differentiated

With TP53 mutation, KRAS & FGFR2 amplification

TP53 mutation					
관련 치료법	US-FDA	US-NCCN	EMA	ESMO	Global Clinical Trials*
MK-1775 + chemotherapy	✕	✕	✕	✕	● (II)
MK-1775 + olaparib	✕	✕	✕	✕	● (II)
ixazomib + vorinostat	✕	✕	✕	✕	● (I)
MK-1775	✕	✕	✕	✕	● (I)
SGT-53, SGT-53 + chemotherapy	✕	✕	✕	✕	● (I)

KRAS amplification					
관련 치료법	US-FDA	US-NCCN	EMA	ESMO	Global Clinical Trials*
selumetinib + chemotherapy	✕	✕	✕	✕	● (II)
sorafenib	✕	✕	✕	✕	● (II)
abemaciclib + LY3214996 , LY3214996 , LY3214996 + chemotherapy, LY3214996 + midazolam	✕	✕	✕	✕	● (I)
BGB-283	✕	✕	✕	✕	● (I)
CB-5083	✕	✕	✕	✕	● (I)
LTT-462	✕	✕	✕	✕	● (I)
LXH254	✕	✕	✕	✕	● (I)

FGFR2 amplification					
관련 치료법	US-FDA	US-NCCN	EMA	ESMO	Global Clinical Trials*
AZD4547	✕	✕	✕	✕	● (II)
dovitinib lactate	✕	✕	✕	✕	● (II)
erdafitinib	✕	✕	✕	✕	● (II)
infigratinib	✕	✕	✕	✕	● (II)
ponatinib	✕	✕	✕	✕	● (II)
ARQ-087	✕	✕	✕	✕	● (I/II)
INCB-54828, INCB-54828 + chemotherapy, INCB-54828 + pembrolizumab	✕	✕	✕	✕	● (I/II)
TAS-120	✕	✕	✕	✕	● (I/II)
FF-284	✕	✕	✕	✕	● (I)
FP-1039 + chemotherapy	✕	✕	✕	✕	● (I)
FPA-144	✕	✕	✕	✕	● (I)
PRN-1371	✕	✕	✕	✕	● (I)

TP53 mutation	
<p>NCT02448329 Study of AZD1775 in Combination With Paclitaxel, in Advanced Gastric Adenocarcinoma Patients Harboring TP53 Mutation as a Second-line Chemotherapy</p> <p>암 유형: 위암 변이 등급: TP53 mutation</p>	<p>다른 식별자: 2014-04-127, Trial/TroveID-257668</p> <p>인구 부분: Second line or greater/Refractory/Relapsed, Stage III, Stage IV</p> <p>제외 기준 변이 등급: ERBB2 amplification</p> <p>단계: II</p> <p>치료법: MK-1775 + chemotherapy</p> <p>장소: Republic of Korea</p>
KRAS amplification	
<p>NCT02448290 Phase II, Single-arm Study of Selumetinib in Combination With Docetaxel, in Advanced Gastric Adenocarcinoma Patients With Low/High MEK Signature, RAS Mutation or RAS Amplification as a Second-line Chemotherapy</p> <p>암 유형: 위암 변이 등급: RAS amplification</p>	<p>다른 식별자: 2014-04-126-010, Trial/TroveID-257645</p> <p>인구 부분: Second line or greater/Refractory/Relapsed, Stage III, Stage IV</p> <p>제외 기준 변이 등급: ERBB2 amplification</p> <p>단계: II</p> <p>치료법: selumetinib + chemotherapy</p> <p>장소: Republic of Korea</p>

MEMO

MEMO