



KUOS 뉴스레터

The Korean Urological Oncology Society

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CONTENTS

제26회 대한비뇨기종양학회 학술대회 2

The 11th KUOS Multidisciplinary Conference 후기 3

집담회소식 20

전이 신장암의 치료제로서 새로이 대두되고 있는 Pazopanib (Votrient®) 에 관한 문헌 고찰 31

공지사항 33

Q 제26회 학술대회 회장 인사말



회원 여러분 안녕하십니까?

2013년 8월 마지막 날 제 26회 대한비뇨기종양학회 정기 학술대회에 회원 여러분을 초대하게 되어 기쁘게 생각합니다.

지난 20년 이상 대한비뇨기종양학회 정기 학술대회는 매년 새로운 지식과 정보를 제공하고 공유하는 장으로서, 때로는 학문적 토의와 논쟁을 통한 발전의 공간으로서 그 역할을 충실히 지켜왔습니다. 지난 학술대회를 통한 회원들의 적극적 참여와 노력은 비뇨기종양 질환 연구 및 학문적 발전의 밑거름으로써 우리 학회의 가장 큰 자량이자 자산이라고 자부합니다.

대구 인터볼고호텔에서 개최하게 되는 이번 학술대회는 전립선암/방광암/신장암의 세 분야로 나누어 국내외에서 활발히 연구하시는 분들을 좌장 및 연자로 모시고 비뇨기종양 분야의 이슈를 정리할 수 있는 시간이 되실 것이라 생각합니다. 또한 Podium session은 지난 1년간 회원 여러분들이 비뇨기종양 분야에 불철주야 연구 하신 성과를 발표하고 서로 토의할 수 유익한 자리가 되리라 생각합니다.

이번 학술대회가 유익한 정보를 나누며 학문적 발전을 도모하는 장이 될 수 있기를 기원하며 회원 여러분의 적극적인 참여를 부탁드립니다.

감사합니다.



대한비뇨기종양학회

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Q 예정 학회 프로그램 안내



▶ 2013년 제26회 대한비뇨기종양학회 정기학술대회 및 총회

- 일 시 : 2012년 8월 31일(토)
- 장 소 : 대구 인터볼고 호텔 엑스코

08:30-09:00	Registration	
09:00-09:10	President's Welcome Congratulatory Remarks	대한비뇨기종양학회 회장 안한중 대한비뇨기과학회 회장 한상원
09:10-09:50	Podium Session I	좌장 : 김형진 (전북의대), 최한용 (성균관의대)
09:50-10:30	Special Lecture Castration resistant prostate cancer: What outcomes do we now want? Epstein RJ (Kingham Cancer Centre, Australia)	좌장 : 안한중 (울산의대)
10:30-10:50	Coffee Break	
10:50-12:00	Interactive debate 1. PSA kinetics is a valuable prognostic tool in localized prostate cancer A, Pros B, Cons 2. Intermittent androgen deprivation is the best treatment for hormone-sensitive prostate cancer A, Pros B, Cons	좌장 : 홍성준 (연세의대), 천준 (고려의대) 정승일 (전남의대) 함원식 (연세의대) 윤석중 (충북의대) 김선일 (아주의대)
12:00-13:00	Lunch	
13:00-13:40	Project 2012 Report / 2013 Proposal	좌장 : 변석수 (서울의대)
13:40-14:20	Podium Session II	좌장 : 김홍섭 (건국의대), 이경섭 (동국의대)
14:20-15:20	Symposium II Treatment of non-muscle invasive bladder cancer 1. Peri-operative intravesical chemotherapy; Is it necessary ? 2. Intravesical BCG instillation maintenance; Which is the best way ? 3. Repeat TURB; When and How ?	좌장 : 김원재 (충북의대), 권동득 (전남의대) 구자현 (서울의대) 강석호 (고려의대) 홍범식 (울산의대)
15:20-15:40	Coffee Break	
15:40-16:20	Podium Session III	좌장 : 유탁근 (울지의대), 전성수 (성균관의대)
16:20-17:20	Symposium III Treatment of renal cell carcinoma 1. RCC with IVC thrombus : Surgical treatment with thrombectomy A, Pros B, Cons 2. Immunotherapy in the era of TKI	좌장 : 김천일 (계명의대), 권태균 (경북의대) 서성일 (성균관의대) 홍준혁 (울산의대) 김태효 (동아의대)
17:20-17:30	2011 KUOS Annual Business Meeting	
17:30-17:40	학술상 시상 및 폐회사 (Adjourn)	

Q The 11th KUOS Multidisciplinary Conference 후기



<http://www.kuos.or.kr>

▶ 사전등록 바로가기

대한비뇨기종양학회

The 11th KUOS Multidisciplinary Conference

| 일시 | 2013년 3월 30일(토) 08:30~17:30 | 장소 | 건국대 새천년 기념관

| 평점 | 대한의사협회 5점

비뇨기종양학회 회원 여러분께

2013년 3월 30일 건국대 새천년 기념관에서 개최되는 11회 Multidisciplinary Conference에 여러분을 초대합니다.

Multidisciplinary Conference는 지난 10년 간 비뇨기종양의 진단 및 치료에 대해 여러 과 선생님들을 모시고 깊이 있는 토론의 장으로서 발전해왔습니다. 올해에도 전립선암과 상부요로상피암을 주제로 최신지견과 생동감 있는 토론이 이루어지도록 준비하였습니다.

11회를 맞이하는 Multidisciplinary Conference에 일본, 대만, 미국의 학술적 업적이 뛰어난 분들을 초빙하여 우리 비뇨기종양학회 회원들과 교류 및 공동연구의 방향을 모색하고자 합니다. 처음 시도되는 international symposium으로 미진한 부분이 있을 것으로 예상되나, 격의 없이 의견을 나누어 아시아 비뇨기종양 연구를 선도하는 모임으로 발전해 나가기를 기대합니다. 경험이 많으신 회원님들의 적극적 참여와 지도를 부탁드립니다.

우리 비뇨기종양학회와 비뇨기병리, 비뇨기영상을 전공하시는 분들 간에 용어 및 진단 기법의 표준화를 위한 작업도 시작하여야 할 때입니다. 이를 위해 이번 Multidisciplinary Conference에서 이점에 대해서도 논의가 있을 예정입니다. 많은 관심과 성원 부탁드립니다.

2013년 한해도 회원 여러분의 건강과 발전이 함께하시기를 기원합니다.

대한비뇨기종양학회 회장 안 한 중

제 11회 KUOS Multidisciplinary Conference 가 2013년 3월 30일 건국대 새천년기념관에서 개최되었다.

이에 앞서 3월 29일에는 국제 연구협력을 위한 미팅이 있었으며 주로 일본과의 종양연구 협력에 대한 의견 교환이 있었다.



비즈니스 미팅사진



학회 후 기념사진

08:30-08:50	Registration	
08:50-08:55	President's Welcome	비뇨기종양학회장 안한중
08:55-09:00	Congratulatory Remarks	대한비뇨기과학회장 한상원
09:00-10:20	International Symposium I: Prostate Cancer	좌장 : 이강현 (국립암센터), Osamu Ogawa (Kyoto Univ, Japan)
	1. Animal models for prostate cancer	Hirotsugu Uemura (Kinki Univ, Japan)
	2. Active surveillance for patients with prostate cancer: Experience in Japan	Yoshiyuki Kakehi (Kagawa Univ, Japan)
	3. Use of PSA in Asian patients with prostate cancer	Yeong-Shiau Pu (National Taiwan Univ, Taiwan)
	4. Establishment of Korean prostate cancer data base	백성현 (건국대의대)
	5. Patient-derived xenografts as useful models for prostate cancer research	Osamu Ogawa (Kyoto Univ, Japan)
10:20-10:40	Coffee Break	
10:40-11:50	Multidisciplinary Session I	좌장 : 김형진 (전북대의대), 이은주 (아주의대 영상의학과)
	Node positive Prostate Cancer	
	1. Imaging for evaluation of L/N metastases	최혁재 (울산의대 영상의학과)
	2. Adjuvant hormonal therapy	강석호 (고려대의대)
	3. Adjuvant radiotherapy	박원 (성균관대의대 방사선종양학과)
	Case Discussion	
	패널 : 강석호 (고려대의대), 박원 (성균관대의대 방사선종양학과), 전황균 (성균관대의대), 최혁재 (울산의대 영상의학과)	
11:50-12:30	International Symposium II: Urothelial Cancer	좌장 : 김세중 (아주의대), Yoichi Arai (Tohoku Univ, Japan)
	1. Photodynamic diagnosis using 5-aminolevulinic acid (5-ALA)	Hideyasu Matsuyama (Yamaguchi Univ, Japan)
	2. Establishment of Korean bladder cancer data base	이형래 (경희대의대)
	3. Prevention of bladder recurrence after nephroureterectomy for upper urinary tract urothelial carcinoma	Yoichi Arai (Tohoku Univ, Japan)
12:30-13:40	Luncheon Symposium	좌장 : 정문기 (부산의대)
	What's the optimal strategy to achieve long term survival in mRCC?	서성일 (성균관대의대)
13:40-14:00	Memorial Lecture	좌장 : 안한중 (울산의대)
	비뇨기과와 비뇨기종양학의 미래	홍성준 (연세의대)
14:00-15:40	International Symposium III: Kidney and Prostate Cancer	좌장 : 천준 (고려대의대), Chikara Ohyama (Hirosaki Univ)
	1. Robotic prostatectomy in East Asia: Learning curve	나군호 (연세의대)
	2. Prognostic systems for renals cell carcinoma in Japan	Kiyohide Fujimoto (Nara Medical Univ, Japan)
	3. Establishment of Korean kidney cancer data base	정진수(국립암센터)
	4. Current status of phase II clinical trial of sorafenib plus IFN-for mRCC patients in Japan	Masatoshi Eto (Kumamoto Univ, Japan)
	5. Prostate cancer-associated alteration of N-glycan on PSA	Chikara Ohyama (Hirosaki Univ, Japan)
	6. Current update in basic research in Korea: Prostate cancer	김원재 (충북대의대)
	7. Cholesterol metabolism in prostate cancer	Jayoung Kim (Dept. of Biomedical Sciences, Cedars-Sinai Medical Center, USA)
15:40-16:00	Coffee Break	

16:00-17:20	Multidisciplinary Session II	좌장 : 최한용 (성균관의대), 기근홍 (조선의대 병리과)
Multidisciplinary Approach of Upper Tract Urothelial Cancer (UTUC)		
1. The role of imaging in UTUC		윤성국 (동아의대 영상의학과)
2. Current updates in pathology of urothelial cancer		조영미 (울산의대 병리과)
3. Practical implementation of ureteroscopy in UTUC		박승철 (원광의대)
4. The role of neoadjuvant and adjuvant chemotherapy in locally advanced UTUC		김호영 (한림의대 혈액종양내과)
Case Discussion		
패널 : 김호영 (한림의대 혈액종양내과), 박승철 (원광의대), 윤성국 (동아의대 영상의학과), 조영미 (울산의대 병리과), 홍준혁 (울산의대)		
17:20-17:30	학술상 시상, 폐회사	

The 11th KUOS Multidisciplinary Conference 요약

<International Symposium I: Prostate Cancer>

1. Animal models for prostate ca
: We have developed a prostate-specific conditional knockout mouse model that targets PTEN using the Cre-loxP system. In this model, mice develop PIN lesions by 8 weeks of age that progress to localized PCa in just 10-15 weeks and to locally invasive PCa with a metastatic rate of 10% at 52 weeks. A short latency combined with 100% incidence rate of PCa makes this model a potential tool for pre-clinical efficacy studies.
2. Active surveillance fir patients with prostate cancer: Experience in Japan
: Since 1999, the Ministry of Health, Labor and Welfare Japan support a multicenter active surveillance study and since 2010, another phase II active surveillance study, the PRIAS-JAPAN, has been launched in conjunction with PRIAS. The results obtained from these studies suggest active surveillance is a safe and reasonable option for low risk prostate cancer
3. Use of PSA in Asian patients with prostate cancer
: Long-term survival outcomes of Taiwanese men based on the screening PSA level shows that the cumulative PCa incidence, PCa mortality and overall mortality rates were higher in men with higher age-referenced PSA percentile values. The age-referenced PSA percentile in a screening population gives useful information in assessing the risk of PCa and PCa mortality.
4. Establishment of Korean prostate cancer data base
5. Patient-derived xenografts as useful models for prostate research
: By evaluation of patient-derived xenografts, we discovered that the prostaglandin receptor EP4 subtype was significantly upregulated during castratin resistance. The analysis of xenograft models with unique clinical course is useful for full explanation of molecular mechanism of the prostate cancer.

<Multidisciplinary Session I: Node positive Prostate Cancer>

1. Imaging for evaluation of L/N metastases

: Although CT and MRI have been used to detect LN metastasis in PCa, the accuracy of them is low to replace surgical staging. MRI with use of ultrasmall particles of iron oxide (USPIO) and Diffusion weighted MRI can detect metastatic LN with right sensitivity. PET CT represents more accurate exam to high-risk PCa, but routine use of it is not yet recommended.

2. Adjuvant hormonal therapy

: 1999년 Messing 및 Estern Cooperative Oncology Group은 근치적전립선절제술 후 골반임파절전이의 소견을 보인 환자들을 대상으로 조기 호르몬 치료의 우월한 결과를 보고하였으나, 2003년 Schroeder 등과 2007년 Spiess 등은 조기 호르몬치료와 후기 호르몬 치료의 결과가 유사하며, 후기호르몬치료가 장기간 치료로 인한 부작용을 피하고, 비용을 절감할 수 있는 장점이 있다고 보고하여 아직 이견이 존재한다.

3. Adjuvant radiotherapy

: 최근 Da pozzo 등은 보고한 후향적 연구에서 수술 후 림프절 전이가 있던 환자에서 HTx alone 군이 HTx + RTx 군에 비해 전립선암에 의한 사망률이 약 2.6배 높았고, 10년 BCR-free survival, Cause-specific survival이 각각 41.7% vs 51.0%, 71.8% vs 70.3%였고 다변량분석에서 adjuvant RTx가 다른 예후인자들과 함께 생존율에 영향을 주는 의미있는 인자임을 보고하였다.

<International Symposium II: Urothelial Cancer>

1. Photodynamic diagnosis using 5-ALA

: The variant fraction of chromosome 9 was significantly higher in fluorescent mucosa (FM) than non-FM, not only for all tissue, but also for non-malignant tissues. These data suggest that a substantial portion of a non-malignant FM harbors alteration of chromosome 9.

2. 비근침윤성 방광 요로상피세포암의 임상양상 및 예후인자 분석: 다기관 연구

3. Prevention of bladder recurrence after nephroureterectomy for upper urinary tract urothelial carcinoma

: In this prospective randomized phase II study, 77 patients were assigned to receive or not receive a single instillation of tetrahydropyranyl-doxorubicin (THP 30mg in 30ml saline). Based on multivariate analysis, THP instillation (HR 0.26) and open surgery (HR 0.28) were independently predictive of a reduced incidence of bladder recurrence.

< International Symposium III: Kidney and Prostate Cancer>

1. Robotic prostatectomy in East Asia: Learning curve

: Various definitions for the learning curve exist and the number of cases needed to surmount. The numbers can be as low as 12 for a reduction of operative time to as high as 500 cases for improvement of functional outcomes. The establishment of a dedicated surgical team will ease the journey through this learning curve.

2. Prognostic system for renal cell carcinoma in Japan

: Recently new prognostic systems based on various combination of tumor stage, performance status, the number/sites of metastases, timing of initial treatment, or lab. The current guideline for clinical

practice of RCC edited by JUA recommends that CRP is useful prognostic factor in pre-treatment stage.

3. Establishment of Korean kidney data base

4. Current status of phase II clinical trial of sorafenib plus INF- α for mRCC patients in Japan

5. Prostate cancer-associated alteration of N-glycan on PSA

: a-2,3-linked sialylation as an additional terminal N-glycan on free PSA is significantly increased in PCa patients compared to BPH patients. Mean fluorescence intensity value were analyzed ROC curve and optimal Cut-off point was determined 1360 for differential diagnosis of PCa. AUC was determined 0.981 much higher than that of conventional PSA test.

6. Current update in basic research in Korea: Prostate cancer

: Urinary cell-free microRNAs (miR-20b, miR-30c-2, miR-361-5p, miR-569, miR-615-3p, miR-711) and nucleic acid (S100A8, S100A9) in urine could be the the valuable diagnostic and prognostic markers in prostate cancer, thus further studies are ongoing. Advanced sequencing technologies have been used to sequence PCa of difference stages.

7. Cholesterol metabolism in prostate cancer

: A variety of signal transduction mechanisms including those propagated by the prosurvival kinase Akt, androgen receptor, IL-6, Stat3, caveolin-1 and other proteins and pathways relevant to PCa involve constituents that localize to cholesterol-rich microdomains. These membrane-associated proteins, and their functional roles, can be altered by changes in circulating cholesterol in vivo.

<Multidisciplinary Session II: Multidisciplinary Approach of Upper tract Urothelial Cancer>

1. The role of imaging in UTUC

: Excretory urography, retrograde pyelogram and US still play a key role in the assessment of hematuria. CT offer superior detection of calculi, urothelial tumor, and parenchymal examination and would become the primary radiologic method of UTUC.

2. Current updates in pathology in urothelial cancer

: 2004 WHO/ISUP grading system, a subclassification of pT3 has been proposed to divide it into pT3a and pT3b. Various clinicopathologic and molecular markers have been proposed to distinguish patients harboring a low-risk disease versus aggressive disease.

3. Practical implementation of ureteroscopy in UTUC

: 현재 많이 사용되고 있는 경성 요관경은 7Fr 이하의 구경을 가지며 2.6Fr working channel을 1-2개 가지고 있다. 구부림이 용이한 연성 요관경은 상부요관과 신장내 집합관을 관찰하는데 용이하며, 7.4-9Fr의 직경과 300도까지의 active tip 굴곡을 가진다. 기술의 발달로 요관경의 사용이 용이해졌으며, 형광물질, narrow band imaging, 그리고 분자표지자의 병합이 정확한 진단과 조기진단을 가능하게 할 것으로 생각한다.

4. The role of neoadjuvant and adjuvant chemotherapy in locally advanced UTUC

: The data from a retrospective study showed that neoadjuvant chemotherapy in high-risk UTUC patients results in a 14% complete response rate and a significant rate of down staging (17% lower pT2 and 20% lower pT3). Adjuvant chemotherapy has been shown in large retrospective studies to have no (or only limited) survival benefit.

01. Uemura

ANIMAL MODEL FOR HUMAN PROSTATE CANCER: PROSTATE-SPECIFIC *PTEN* CONDITIONAL KNOCKOUT MOUSE

Hirotsugu Uemura, M.D.Ph.D.
Department of Urology
Kinki University Faculty of Medicine
Osaka-Sayama, Japan

Summary

- GEMM models provide an invaluable tool for drug discovery.
- Conditional *Pten*-knockout mice serve as an efficient model to study deregulated signaling pathways associated in prostate carcinogenesis.

Future Directions

- Target additional altered signaling pathways
- Combinatorial treatment strategies
- Develop a drug resistance model
- Identify prognostic or therapeutic biomarkers

02. Kakehi

Active Surveillance for Low Risk Prostate Cancer -Experience in Japan-

Yoshiyuki Kakehi, M.D., D.Med. Sci.
(Dept. of Urol., Kagawa Univ. Fac. of Med.)

1st East Asian Genitourinary Oncology Meeting

Conclusions

- Several phase 2 including the 2 Japanese studies indicate that AS is a safe and feasible treatment strategy for low risk prostate cancer to avoid overtreatment.
- Underestimation at the initial Dx is so far inevitable, which demands new markers and high-quality imaging.
- p2PSA and its related parameters are promising for accurate patients' selection for AS.

03. Pu

Use of PSA in Asian Patients with Prostate Cancer

Yeong-Shiau Pu (蒲永孝), MD, PhD, EMBA

Director and Professor, Department of Urology,
National Taiwan University Hospital
Chairman, Uro-Oncology Committee, Taiwan Urological Association

2013-March-30
1st East Asian Genitourinary Oncology
Seoul, Korea

Take Home Messages

- Prostate cancer is on the rise in Asia.
- Asian men tend to have higher PSA levels and more unfavorable prognostic features at cancer diagnosis.
- The biological implications of elevated PSA may be different across ethnic groups.
- The role of PSA screening in Asian men is yet to be demonstrated.
- Taiwanese (Asian) men with an age-referenced PSA >the 99th percentile are at an increased risk of PC death than men with lower percentile levels.
- The age-referenced PSA percentile values may be a useful tool to predict PC death in a screened population.

04. 백성현

ESTABLISHMENT OF KOREAN PROSTATE CANCER DATABASE

Konkuk University

Sung Hyun Paick

Expected progression

- Korean prostate cancer database program will proceed continuously
- Protocol will be changed: add more contents and changed to E-CRF form
- Data collection at 2013: data from 2006 to 2010
- Data collection at 2014: data from 2011 to 2013, whole data update
- At 2015, Program will be changed from retrospective to prospective study → become a real register program

05. 최혁재

Node Positive Prostate Cancer: Imaging for Evaluation of LN Metastasis

Hyuck Jae Choi

Department of Radiology
Asan Medical Center

Conclusion

- Knowledge of clinical anatomy and pathway
 - Key to accurate interpretation
- Presurgical detection of LN metastasis
 - MRI based morphologic evaluation ↓
 - PET/CT ↓

Conclusion

- Recent advances
 - DW MRI
 - USPIO MRI
 - Choline PET
 - Promising
 - Little number of study done
 - Lower spatial resolution
 - False negative
- Other strategy needed
 - Biologic and clinical combined evaluation
 - Fusion of multiple modality

06. 강석호

-Node Positive Prostate Cancer- **Adjuvant Hormonal Therapy**

Seok Ho Kang
Department of Urology
Korea University College of Medicine



□ Conclusions (1)

- There is no optimal treatment for node+ prostate cancer because of lacking large randomized trial.
- The treatment options are very wide from observation to hormonal therapy, surgery, radiation, or any combination of these treatment
- Disease control is possible in some patients with surgery, radiation, or hormones alone.
- Long term durable has been expected with hormonal therapy after surgery or radiation



□ Conclusions (2)

- The exact timing of hormonal therapy is still uncertain.
- One reasonable approach is to treat the prostate with surgery and/or radiation. Hormonal therapy can be used as an early adjuvant therapy or at the time of PSA elevation.
- It is clear that many questions regarding node+ pca will remain unanswered without more randomized clinical trial.



07. 박원

Adjuvant Radiotherapy

Samsung Medical Center
Won Park

Conclusion

-the role of adjuvant radiotherapy for pN(+) patients: no answer

However,

-increase treatment results in high-risk patients with adjuvant radiotherapy
-high biochemical failure in pN1 patients treated with adjuvant hormonal therapy
-can reduce the radiation toxicities with IMRT and IGRT

-so, adjuvant RT might be considered in pN1 patients with hormonal therapy

-prospective multi-center randomized trial will be needed

08. 전립선암증례토론

Case Discussion

좌장: 김영진 (전북의대), 이은주 (아주의대 영상의학과)

패널: 강석호 (고려의대), 박원 (성균관의대 방사선종양학과),
최혁재 (울산의대 영상의학과), 전황균 (성균관의대)

Case 1

M/50

C.C : High PSA (10.31 ng/mL)

DRE : 20g, firm, not tender, palpable nodule at lt. lobe

Case 2

M/54

C.C : frequency

DRE : 30g, firm, not tender, palpable nodule at lt. lobe

PSA : 10.07 ng/mL

09. Matsuyama

Clinical significance and cytogenetic analysis of false positive mucosa of the photodynamic diagnosis (PDD) using 5-aminolevulinic acid (5-ALA)

Hideyasu Matsuyama

Department of Urology, Graduate School of Medicine,
Yamaguchi University



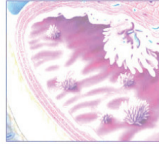
Department of Urology, Graduate School of Medicine, Yamaguchi University

Conclusion

- PDD is promising modality for the detection of flat tumor with acceptable sensitivity, but low specificity due to false positive cases.
- Substantial number of false positive case may result from premalignant chromosomal 9 aberrations.
- PDD-assisted TUR may improve patient outcome in T1/high grade non muscle-invasive bladder cancer.

10. 이형래

Establishment of Korean Non-Muscle Invasive Bladder Cancer Data Base



Hyung-Lae Lee MD. PhD
Kyung Hee University School of Medicine,
Seoul, Korea



Conclusions



- It is meaningful that this study is the first nationwide study for NMIBC in Korea.
- Because there were a few incomplete or omitted data, the cooperation and effort of colleagues are needed.
- The data used in this study will serve as the starting point for ongoing data compilation.



Conclusions



- Although there may be several reasons as to why they hadn't, some patients with T1 high grade didn't receive BCG therapy.
- BCG induction therapy and maintenance therapy have the merits of preventing recurrence and progression in patients.



11. Arai

Prevention of bladder recurrence after nephroureterectomy for upper urinary tract urothelial carcinoma



Yoichi Arai, M.D., Ph.D.
Tohoku University Graduate School of Medicine
Tohoku Urological EBM Study Group, JAPAN

Conclusions

- In this prospective randomized Phase II study, a single intravesical instillation of THP immediately after NUx is the effective treatment for preventing consequent bladder recurrences.
- In order to confirm therapeutic efficacy of this treatment, Phase III trial in a large-scale multicenter analysis should be necessary.

Ito A, Arai Y, et al. J Clin Oncol (Epub ahead of print)

12. 서성일

Optimal Strategy in the Treatment of mRCC
what's new in first-line therapy

서 성 일
삼성서울병원

Take home message

- Until the results of the CARMENA trial are available, surgery should remain an important part of the treatment strategy in the era of TA
- So far, no reliable predictive factors available to facilitate choice in first-line favourable/intermediate risk patients
- Study design of PISCES and COMPARZ undermine reliability of results in terms of efficacy, QoL- and patient's preference→personal experience remains the most important factor for individual treatment decision
- New promising agents may further complicate the treatment algorithm (but benefit the patient)

13. 나균호

**Robotic Prostatectomy in Asia
- Overcoming the Learning Curve**

KH Rha
Yonsei Univ
Seoul, Korea


Conclusion

- 30 cases appear to be the number of cases need to overcome the learning curve with regards to perioperative outcomes.
- In terms of functional outcomes, larger number of cases are needed. Exact number of cases is controversial. The more the merrier?
- A dedicated robotic team is essential !


14. Fujimoto

The 11th KJON Multidisciplinary Conference and the 1st East Asian Genitourinary Oncology Meeting
30 March, 2013, New Millennium Hall, Konkuk University, Seoul

Prognostic systems for patients with renal cell carcinoma in Japan




Kiyohide Fujimoto
Nara Medical University &
Nara Urological Research & Treatment Group (NURTG)



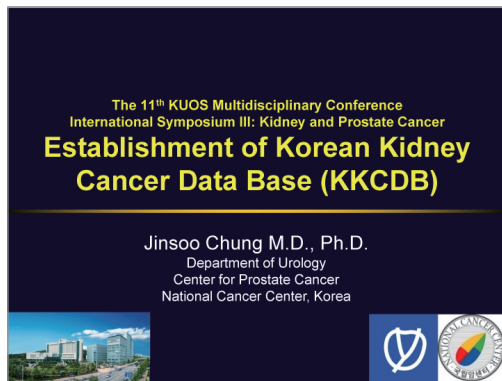
Conclusions

I have not yet realized enough clinical value of prognostic systems.

More prospective studies using these prognostic system are needed to elucidate their true clinical significance in the era of targeted therapy.



15. 정진수



Past and present status of RCC in Korea : summary and task

- Epidemiology of RCC
 - stage migration (↑SRM, ↑incidentaloma)
 - improved prognosis and survival rate, recent days
- Current management of localized RCC
 - wide use of nephron sparing surgery with minimal invasive surgery
- Current management of mRCC
 - paradigm shift from Cytokine therapy to Targeted therapy
- Tasks for present status of RCC in Korea
 - no nationwide survey or data for recent changes of RCC in Korea
 - *recent natural history, difference in treatment outcomes & prognosis, improved survivals of mRCC...
 - only several single institute and multicenter studies available
 - **need nationwide survey**

국립암센터
NCCN, Korea, 2013

16. Eto

Current Status of Phase II Clinical Trial of Sorafenib Plus IFN-α for mRCC Patients in Japan

Masatoshi Eto¹, Go Kimura², Nobuo Shinohara³,
Shiro Hinotsu⁴, Katsunori Tatsugami⁵, Seiji Naito⁵,
and Japan RCC Trialist Collaborative Group (JRCTG)

¹Kumamoto University, Kumamoto, Japan
²Nippon Medical School, Tokyo, Japan
³Hokkaido University, Sapporo, Japan
⁴Okayama University, Okayama, Japan
⁵Kyusyu University, Fukuoka, Japan

1st East Asian Genitourinary Oncology Meeting, @the Millenium Hall, March 30, 2013

Summary

In our experiments of interferon-α + sorafenib combination therapy :

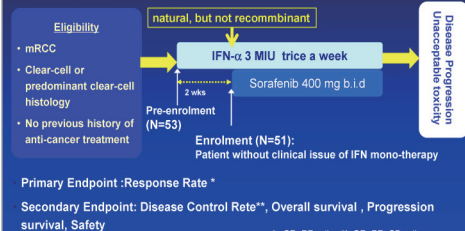
- Enhanced induction of apoptosis for tumor cells *in vivo*
- Induction of CTL and NK activity *in vivo*

were demonstrated, implicating the rationale for good results of clinical trials with interferon-α + sorafenib combination therapy (JCO 25:3288, 2007).

Multi-Center Phase II Clinical Trial on Efficacy and Safety of Interferon Alfa-n1 + Sorafenib Combination Therapy in Renal Cell Carcinoma

Study Group: JRCTG (Japan RCC Trialist Collaborative Group)

Study design: Open label, Single arm, Multi-center, Phase II



Major Eligibility Criteria

≥ 20 years

Patients with confirmed clear cell renal cell carcinoma

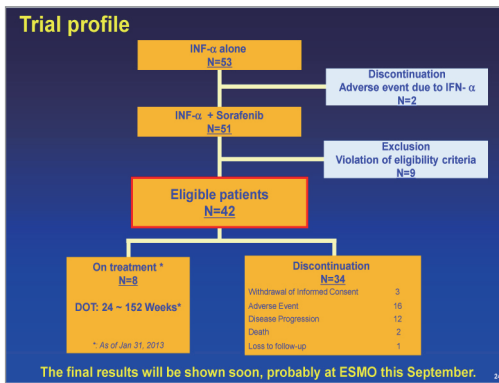
History of nephrectomy

No previous history of chemotherapy, cytokine therapy, or molecularly targeted drug therapy (however, patients using IFN alfa as post-nephrectomy adjuvant therapy will be eligible if not used for 6 or more months)

ECOG PS 0 or 1

At least 1 measurable lesion on CT, as defined by RECIST

Adequate organ function (Renal, liver, hematopoietic function and coagulation system)



17. Ohyama

HIROTSAKI UNIVERSITY

Prostate cancer-associated alteration of N-glycan on PSA

Development of new assay system detecting aberrant PSA glycosylation

Chikara Ohyama
Urology
Hirotsaki University

HIROTSAKI UNIVERSITY

Conclusions

- PSA is a Glycoprotein.
- Cancer-associated PSA is rich in **Sialic acid-2,3Galactose** residue.
- Glycan-targeted novel PSA assay system with higher specificity may be promising.

18. 김원재

CHUNGBUK NATIONAL UNIVERSITY HOSPITAL

Current Update in Basic Research in CBNU: Prostate Cancer

Wun-Jae Kim
Department of Urology
Chungbuk National University

S100A8/9 in CaP: Conclusions

- Expression levels of S100A8/9 are decreased in CaP tissues than BPH
- S100A8/9 are highly expressed in patients with high PSA and metastatic stage than those with low PSA and localized stage
- Urinary S100A8/9 are decreased in CaP patients than BPH
- Urine might represent S100A8/9 expression status in cancer tissue.
- However, reproducibility and stability should be validated.

충북대학교병원

Ongoing Research from Urine

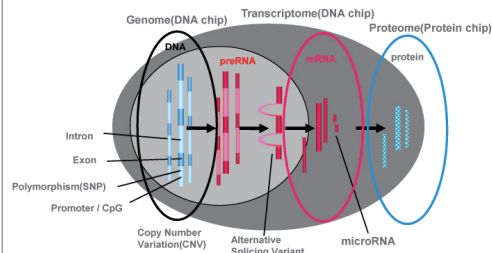
- Candidate genes of RNA expression levels from GEO data (GSE6919)

Candidate Genes	BPH	CaP
1	1.026879	2.33576
2	0.366117	2.00468
3	0.973111	3.08653
4	1.046136	3.40889
5	1.052093	3.21009
6	1.059629	2.82713
7	1.037675	2.67148
8	1.142899	2.66993
9	1.090051	2.31418
10	0.86865	2.23425
11	0.659818	2.18425
12	0.795873	2.0575
13	0.957624	2.02254

➔ Detection of Nucleic acid from Urine

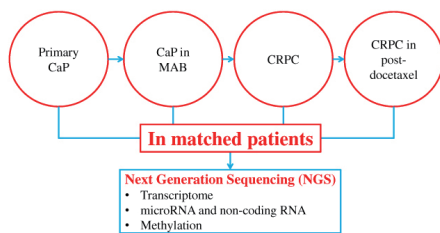
충북대학교병원

Future Directions: Genomic Approach & Gene Regulation using NGS



충북대학교병원

Future Directions: Genomic Approach & Gene Regulation using NGS



충북대학교병원

19. kim jay

Cholesterol Metabolism and Prostate Cancer

Jay Kim
Harvard Medical School
Cedars-Sinai Medical Center

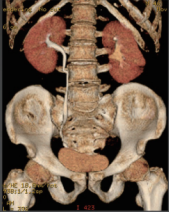


Summary

- Hypothesis:** Cholesterol enhances AR signaling in prostate cancer metastasis by epigenetic, metabolic and intracrine mechanisms.
- Circulating level of cholesterol and prostate cancer
- Molecular mechanism: Lipid raft microdomains
- Lipid metabolism and prostate cancer

20. 윤성국

**The Role of Imaging
in Upper Tract Urothelial Cancer**



Seong Kuk Yoon
Department of Radiology
Dong-A Medical Center
Dong-A University College of Medicine

Conclusions

- MDCTU offers superior detection of UTUC over EU and US and allows accurate staging.
- Accurate radiologic detection and staging of UTUC is essential to determine appropriate treatment.

21. 조영미

**Current Updates in
Pathology of UTUC**

울산의대 서울아산병원
병리과 조 영미

Upper Tract Urothelial Cancer

- Grading
- Staging
- Prognostic factors
- Lynch syndrome



22. 박승철

The 11th KUOS Multidisciplinary Conference

Multidisciplinary Session II.



**Practical Implementation for
Ureteroscopy in UTUC**

Seung Chol Park
Wonkwang University School of Medicine and
Hospital

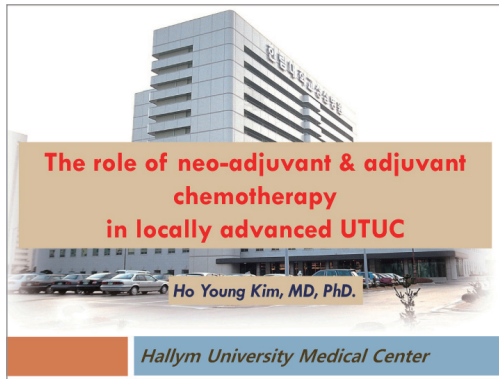



Take Home Message

- Ureteroscopy
 - Diagnostic uncertain
 - Conservative treatment
- No touch diagnostic ureteroscopy
 - Essential technique
- Technological advances
 - Efficient flexible ureteroscopy
 - Improved visualization
 - Fluorescence
 - Narrow band imaging
- Ureteroscopic treatment another acceptable option

23. 김호영



Conclusions

- Commitment to clinical research with pragmatic clinical trial designs
- A multidisciplinary approach and better collaboration among urologists, oncologists, radiation therapists, basic researchers, advocacy networks, and industry is critically important.

24. 요로상피암 증례토론

Case Discussion

좌장: 최한용 (성균관의대), 기근홍 (조선의대 병리과)
 패널: 김호영 (한림의대), 박승철 (원광의대),
 윤성국 (동아대의대 영상학과),
 조영미 (울산의대 병리과), 홍준혁 (울산의대)

Case 1

F/58

C.C : Incidentally detected Rt. Hydronephrosis
 on f/u CT scan for ovarian cancer

P/hx: TAH c BSO with adjuvant CTx for ovarian ca., 6YA

U cytology: negative

Case 2

F/54

C.C : gross hematuria

U/A: RBC many/HPF, WBC 0-2/HPF

● 대한비뇨기종양학회지 학술상 시상내역

대한비뇨기종양학술지 게재 논문 우수 학술상은 다음과 같습니다.

1) 기초 부문

제목: IRAK4 유전자다형성과 전립선암 감수성과의 상관성

저자: 김해종, 이재혁, 한준현, 이지열, 장인호, 김태형, 김경도, 명순철

대한비뇨기종양학술지 201210:27-33

2) 임상 부문

제목: 전립선암의 호르몬 불응성과 PTEN, CD44 발현양상의 연관성 분석

저자: 함원식, 박재원, 조강수, 이창기, 최영득, 홍성준

대한비뇨기종양학술지 2012;10:21-6

Q 집담회 소식



[대한비뇨기종양학회 집담회 개최 안내]

대한비뇨기종양학회 집담회가 화순 전남대병원에서 개최될 예정입니다.
집담회 후에는 회식도 준비 되어 있습니다.

좋은 봄 날씨에 멋과 맛의 고향 화순에서 비뇨기종양에 대한 고견도 주시고 맛깔스러운 전라도 음식에 정담을 나누실 수 있는 기회입니다. 많은 참석을 부탁드립니다.

* 집담회 준비를 위해 참석하실 분은 **신청서**를 보내주시길 부탁드립니다.
(성명, 소속, 연락처를 기재하셔서 이메일로 보내주시면 됩니다. app@app2010.com)

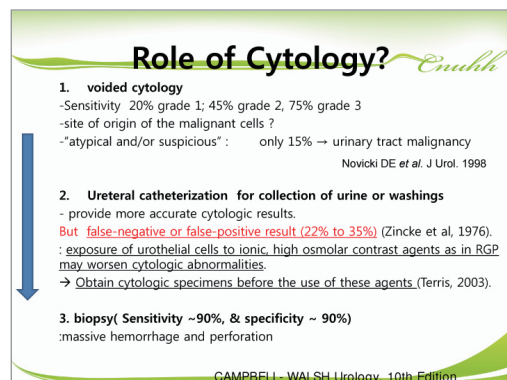
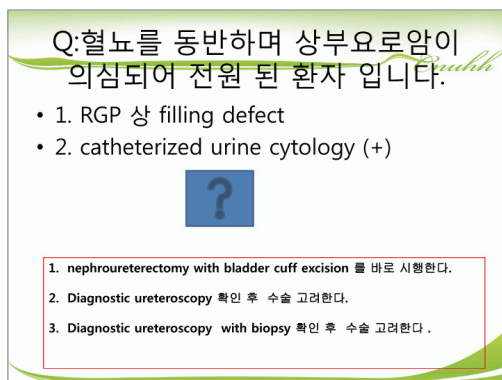
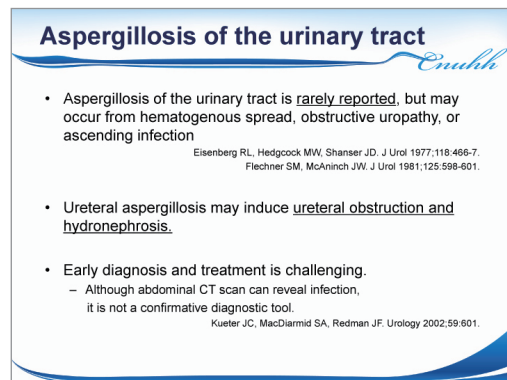
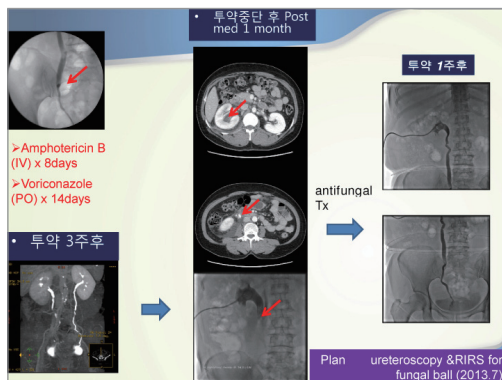
- 일시: 2013년 5월 31일(금) 18:00-19:10

- 장소: 화순 전남대병원 지하대강당

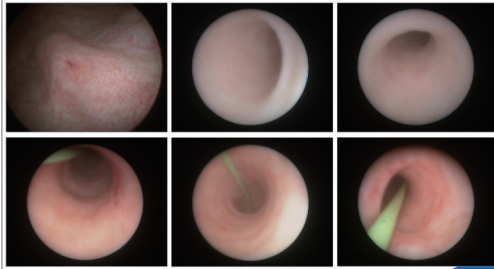
Time	Subject	Speaker	Moderator
18:00-18:05	Opening remark	안한중 회장	조진선 학술이사
18:05-19:05	Case presentation & Brief Review Case 1:상부요로상피암과 감별이 필요한 질환 Case 2:전립선에 발생한 요로상피암	전남대 정승일 충남대 임재성	울지대 김대경
19:05-19:10	Closing remark	안한중 회장	조진선 학술이사



정승일 증례발표내용



Diagnostic URS, Rt. (2013.2.4)



Case Summary

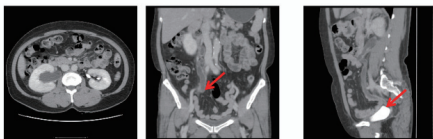
Imaging : Rt. Hydro & distal ureteral mass ??
 Ureteroscopy OP finding
 - Bladder 내부 특이소견 없음.
 - Rt. ureter 내부 특이소견 없음. Normal mucosa
 Cytology
 - Bladder: benign atypia
 - Rt. Ureter: suspicious for malignancy
 Urine Tbc study (-)
 Imp. R/O Ureter tumor, Rt.
 Plan 1개월 후 Lab, APCT(IVP), urine cytology

Abdomen-pelvic CT (2013.2.26)

2013.2.25 (POD 21)

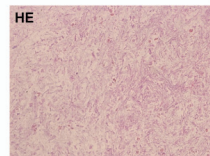
- RLQ pain, fever (-)

1. More aggravation of wall thickening at right distal ureter, considered as **aggravation of R/O urothelial malignancy**.
2. Aggravation of obstructive uropathy in right.
3. Tiny GB stone.

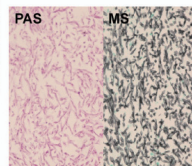


RLQ pain → Self voiding 시 배출된 tissue
 Pathologic diagnosis 의뢰

Self voiding 시 배출된 tissue
 Pathologic diagnosis
 : Fungal ball, morphologically Aspergillosis



from Google image



MS: methenamin silver stain
 PAS: Periodic acid schiff

투약 중단 후 Post med 1 month

투약 1주후

antifungal Tx

투약 3주후

Plan ureteroscopy & RIRS for fungal ball (2013.7)

> Amphotericin B (IV) x 8 days
 > Voriconazole (PO) x 14 days

Aspergillosis of the urinary tract

- Aspergillosis of the urinary tract is **rarely reported**, but may occur from hematogenous spread, obstructive uropathy, or ascending infection

Eisenberg RL, Hedgcock MW, Shanser JD. J Urol 1977;118:466-7.
 Flechner SM, McAninch JW. J Urol 1981;125:598-601.

- Ureteral aspergillosis may induce **ureteral obstruction and hydronephrosis**.

- Early diagnosis and treatment is challenging.
 - Although abdominal CT scan can reveal infection, it is not a confirmative diagnostic tool.

Kueter JC, MacDiarmid SA, Redman JF. Urology 2002;59:601.

Aspergillosis of the urinary tract

- Urine cultures may not find Aspergillus.
- The fungal ball can be treated effectively by **surgical resection and antifungal pharmacotherapy**.
- Endoscopic management** through either an antegrade or a retrograde approach is also effective.
 Modi P, Goel R. Urol Int 2007;78:374-6.
- Small fungal balls can be treated with antifungal drugs before surgery.
 Smaildone MC, Cannon GM, Benoit RM. J Endourol 2006;20:318-20.

CASE - 2



외원진료대학병원

조 O O (F/42)

C.C. Right back ~ abdomen pain (D: 1 month)

P.I. 1개월간의 Rt. flank~abdomen pain 주소로 local 내원하여 시행한 US, APCT 에서 Hydronephrosis, Rt. 및 Rt. lower ureter의 filling defect 관찰되어 본원 내원.

P.Hx. DM/HTN (-/-), C-sec ('04, '06)

V/S N-S

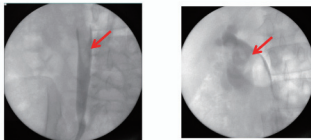
LAB CBC 7,200 / 11.9 / 464K
UA RBC -, WBC -
other Lab N-S

Abdomen-pelvic CT (2011.10.7 local)



1. nephroureterectomy with bladder cuff excision 를 바로 시행한다.
2. RGP with cytology 시행한다
3. Diagnostic ureteroscopy 확인 후 수술 고려한다
4. Diagnostic ureteroscopy with biopsy 확인 후 수술 고려한다

RGP, Rt. (2011.10.25)



Urine cytology (bladder, Rt. Ureter)
Benign atypia

1. nephroureterectomy with bladder cuff excision 를 바로 시행한다.
2. Diagnostic ureteroscopy 확인 후 수술 고려한다
3. Diagnostic ureteroscopy with biopsy 확인 후 수술 고려한다

상부요상피암이 의심이 되는 모든 경우 ureteroscopy (with or without biopsy) 가 필요한가요?

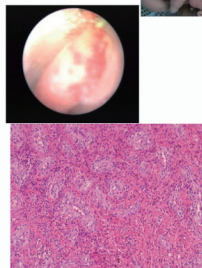
- 1. No
- 2. Yes

- Tx:
 - 1) Diagnosis (??) after conventional radiographic studies
 - 2) Tx plan may be modified on the basis of the ureteroscopic findings (e.g. endoscopic resection)
- risks of tumor seeding, extravasations, and dissemination are low, but these risks are real
→ should preclude ureteroscopy when it is unnecessary

CAMPBELL - WALSH Urology, Tenth Edition

Diagnostic URS, Rt. (2011.11.23)

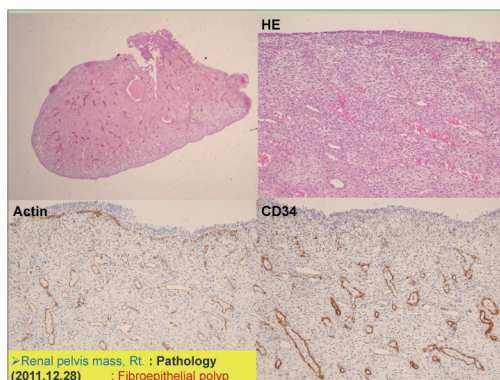
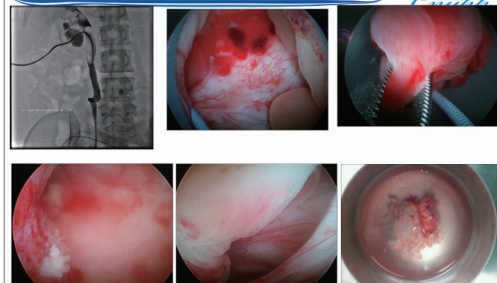
- Rt. mid ureter 상방으로 elongated mass 존재하며 renal pelvis 에서 기원함.
- Frozen biopsy 상 benign 소견 보여 tumor 일부 요관경하 Holmium laser 이용하여 절제.



➤ Renal pelvis mass, Rt.

: Suggestive for Fibroepithelial polyp

Percutaneous renal pelvis tumor excision (2011.12.28)



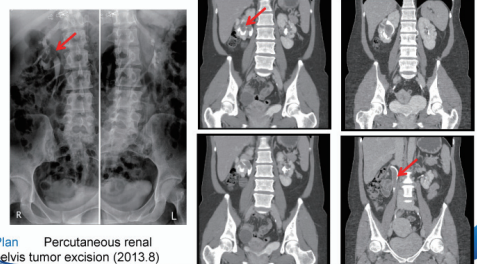
➤ Renal pelvis mass, Rt. : Pathology (2011.12.28)
: Fibroepithelial polyp

조 O O (F/42)

(5months f/u)

(8months f/u)

(15months f/u)



Plan Percutaneous renal pelvis tumor excision (2013.8)

Fibroepithelial Polyp

- Most common benign neoplasm of the Ureter.
- Mean age at Dx: 40 yrs. (7-73 yrs)
- Male > Female (3:2), Adults > Pediatrics
- Ureter & UPJ ($\approx 60\%$, Lt > Rt)
 - > Renal pelvis > Bladder, posterior urethra
- Unilateral, Solitary \gg Bilateral, Multiple
- Symptoms: Flank pain, Hematuria, dysuria
No symptom ($\approx 40\%$)

Fibroepithelial Polyp

- Etiology
 - mesodermal origin
 - associate with "Urolithiasis", UPI obstruction, ureteral stenting and recurrent UTI.
 - No risk factors ($\approx 40\%$)

Treatment

Nephroureterectomy
Ureterotomy
Dismembered pyeloplasty
Segmental resection c ureteroureterostomy
Ureteroneocystostomy

→ "Endoscopic management"
: Local coagulation by laser (Ho:YAG)
Percutaneous antegrade excision
Laparoscopic surgery

J Endourol. 2009;23(9):1415- 9

CASE - 3,4,5



김 O O (58/M)

C/C: Painless gross hematuria (onset : 12days ago)

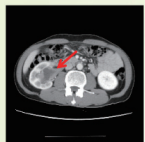
P/H: No known Hx of DM, Pul Tb, Hepatitis
HET med 중

P/I: 상기자 4월 7일경 Painless gross hematuria 있어 타병원 내
원하여 시행한, Abdomen CT 상, TCC 의심소견 보여 내원함.

Lab

<U/A> WBC >100/ HPF RBC 1-4
<Cr> 1.1

<Abd CT> #2010.04.08



• <U/A> WBC >100/ HPF RBC 1-4
antibiotics medication 1 week

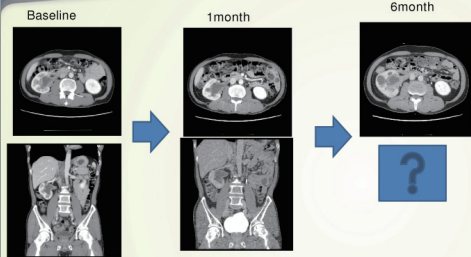
- U/A: WBC - Microscopy:20-29 [0~4]
RBC:0-1 [0~1]
- MTB PCR Hybridization: Negative
- AFB stain: positive
- Urine culture: negative
- Tb culture: negative (6.16)
- Urine cytology: negative



2010.5.20 antiTbc medication start

Post medication 3 month
• U/A WBC - Microscopy:5- 9 [0~4]
RBC:1- 4 [0~1]

Post antiTbc medication



Renal scan
LK: RK split renal function =
81 : 19

Impression

1. Urinary Tbc infection
2. R/O renal pelvis tumor. Rt
3. Non functioning kidney Rt.

Op: laparoscopic Rt. nephroureterectomy
with bladder cuff excision

NON- INVASIVE PAPILLARY
UROTHELIAL CARCINOMA, HIGH
GRADE (pTa)



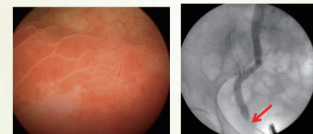
모 O O O (72/F)

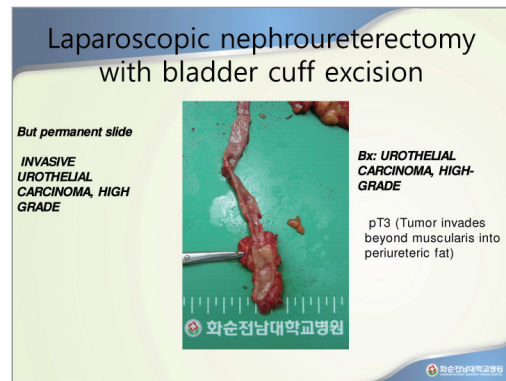
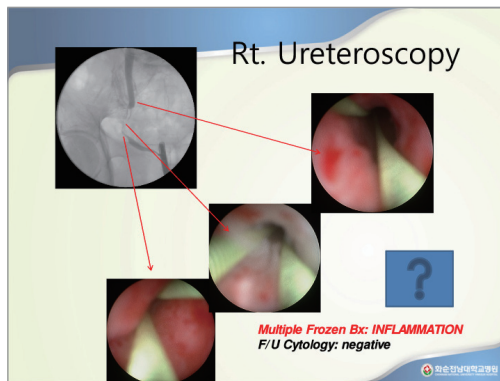
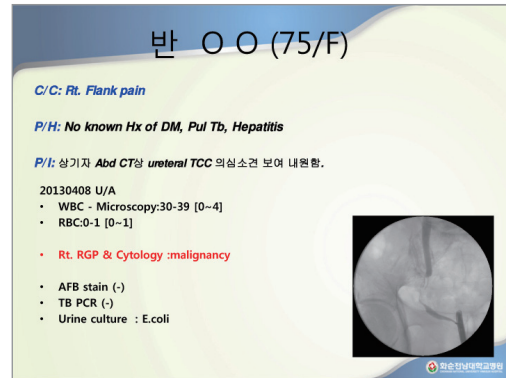
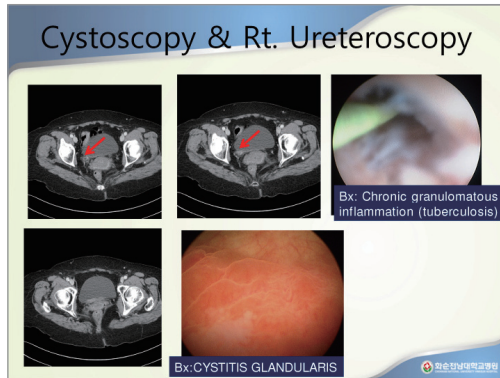
C/C: Rt. Hydronephrosis
bladder mass

P/H: No known Hx of DM, Pul Tb, Hepatitis, HET

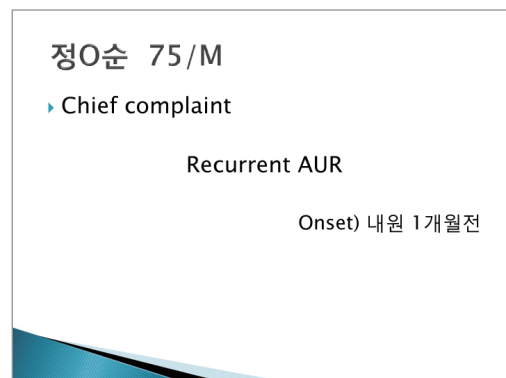
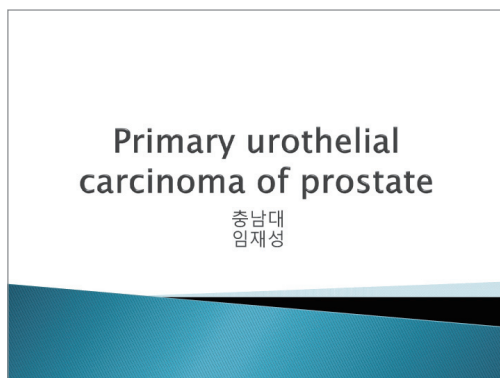
P/I: 상기자 검시야 병변 내원하여 시행한, US 및 cystoscopy' TCC 의심소견 보여 내원함.

- WBC :10-19 [0~4]
- RBC:1-4 [0~1]
- Cytology: negative
- AFB stain (-)
- TB PCR (-)





임재성 증례발표내용



> Present illness

- 내원 3년부터 local에서 BPH medication
- 내원 약 1달 전 부터 AUR 지속되어 본원 내원.

< Past medical history >

DM / HTN / Pulmonary TB / Hepatitis (- / + / - / -)
HTN - 5년 전 진단, medication (+)
no major op Hx.

< Social history >

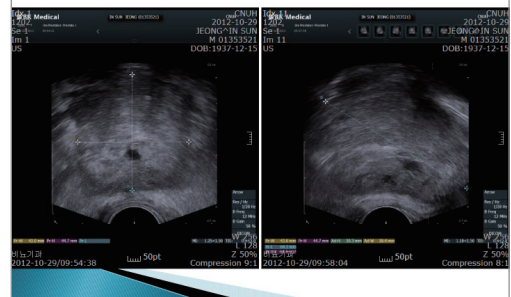
Drinking : (-)
Smoking : (-)
Herb : (-)

< Physical Examination >

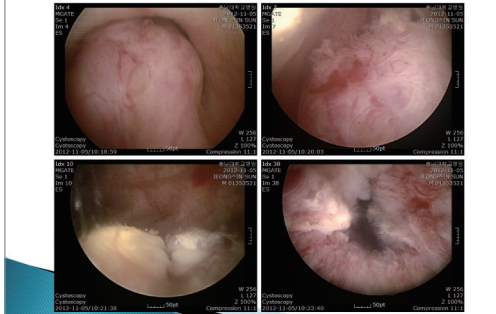
> DRE

- Both lobe) hardness
- No tender & no nodularity

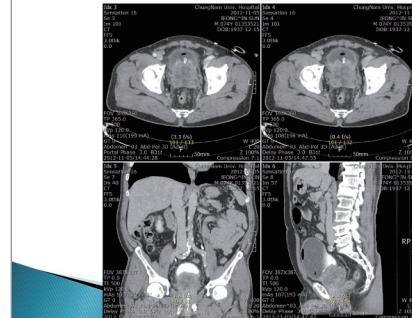
TRUS



Cystoscopy



CT



< Problem List >

#1. Recurrent AUR

T-P) TUR-P

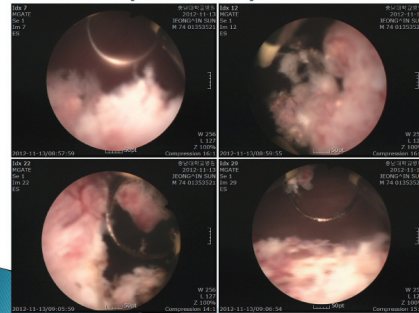
< Hospital course >

< TUR-P (12.11.13) >

Operation Finding

- bladder neck 부터 prostatic urethra까지 mass lesion이 관찰되었다.
- bladder neck elevation이 관찰되었고 non-movable하였다.
- bladder 내에는 trabeculation 외에 특이소견은 관찰되지 않았다.

< TUR-P (12.11.13) >



< Biopsy >

조직병리학적검사결과지

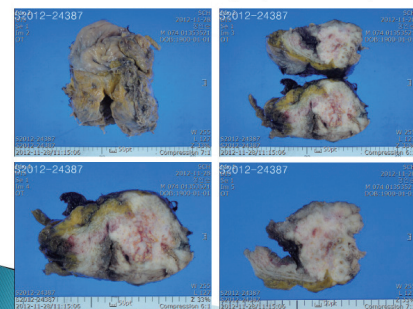
◎ 육안 소견

Specimen consists of multiple fragments of soft tissue, measuring 0.8x0.5cm in size of the largest one.

◎ 병리진단

TUR-P:
Infiltrating urothelial carcinoma, high grade.

< Plan : Bricker's op (12.11.22) >



< Biopsy >

조직병리학적검사결과지

◎ 육안 소견

Specimen consists of three parts as follows:

No.1: Specimen consists of a radical cystectomized urinary bladder attached with a prostatic and both seminal vesicles, measuring 10x12x10cm in size and 482g in weight. There is an irregularly elevated lesion in the urinary bladder, measuring 3x4cm in size. The main mass infiltrate to the prostate. Both ureters are attached, measuring 5.5cm and 5cm in length, respectively (A1-A22).

No.2: Specimen labeled "right pelvic lymph node" (B).
No.3: Specimen labeled "left pelvic lymph node" (C).

◎ 병리진단

Urinary bladder, bricker's operation:
Infiltrating urothelial carcinoma, high grade (A1, A3-A6, A9-A10 & A13-A22), with
1) invasion to the prostate and seminal vesicle
2) tumor emboli in lymphovascular spaces, multiple
3) no lymph node invasion (B & C)

이오우 70/M

▶ Chief complaint

Recurrent AUR

Onset) 2012년 11월 11일

2012년 11월 16일

▶ Present illness

- 2009. 8월 local 통해 TURP 시행 받음.
(수술 전 PSA 1.54)
- 당시 조직검사 결과
nodular hyperplasia
- 2011년 11월 2차례 AUR로 본원 응급실 통해 foley cath keep (당시 alcohol, URI medication Hx는 없었음.)
- urgency, dysuria 지속됨.

< Past medical history >

DM / HTN / Pulmonary TB / Hepatitis (- / - / - / -)
내원 10여년 전 선병원 통해 rectal ca. 로 open surgery
내원 3년 전 선병원 통해 stomach ca. 로 op.
내원 3년 전 본원 OS 통해 Lt. hand op.

< Social history >

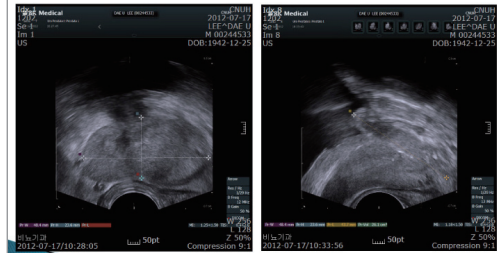
Drinking : (-)
Smoking : (-)
Herb : (-)

< Physical Examination >

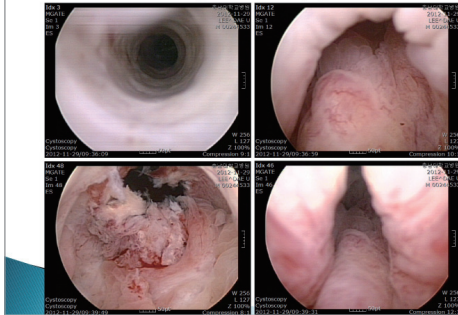
DRE

- Smooth & firm
- No tender & no nodularity

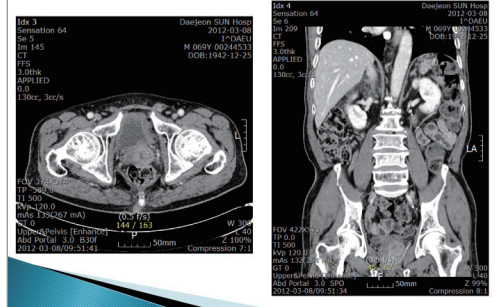
TRUS



Cystoscopy



CT



< Problem List >

- #1. Recurrent AUR
- #2. voiding Sx (urgency, dysuria)

T-P) palliative TUR-P

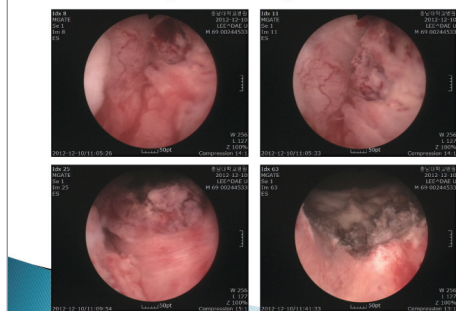
< Hospital course >

< TUR-P (12.12.10) >

Operation Finding

- urethral stricture로 21Fr-27Fr metal soundation 시행하였다.
- bladder neck, prostatic urethra에 multiple papillary mass 가 관찰되어 각각 따로 Bx 시행하였다.
- prostatic urethra가 irregular하였으며 조직이 fragile하고 hypervascularity가 관찰되었다.
- bladder 내에는 trabeculation 외에 특이소견은 관찰되지 않았다.

< TUR-P (12.12.10) >



< Biopsy >

조직병리학적 검사결과지

◎ 육안 소견

Three specimens are received as follows:

No.1: Specimen labeled "prostate main" consists of multiple fragments of soft tissue, weighing 3.5g in the aggregate (A1,A2).

No.2: Specimen labeled "prostate mass" consists of multiple fragments of soft tissue, weighing 1.5g in the aggregate (B).

No.3: Specimen labeled "bladder neck" consists of three fragments of soft tissue, measuring 1.0x0.3cm in size of the largest one (C)

◎ 병리 진단

Prostate and bladder neck, TUR-P;

Urothelial carcinoma (A1,A2,B.)

* Immunohistochemical staining results (B);
1) PSA, negative. 2) AMACR, focal positive. 3) CK-7; negative.

< Plan >

- ▶ Radical cystectomy
- ▶ 보호자 원하여 서울로 전원.

임재성 Review of topic

Urothelial Carcinoma of the Prostate

Classification

Table 1 - Classification of prostatic involvement according to Hardeman and Soloway [29]

Stage 1	Tumor confined to prostatic urethelium
Stage 2	Invasion of ducts and acini but confined to the basal membrane
Stage 3	Stromal invasion

Table 2 Staging of patients with bladder cancer and prostatic involvement according to the TNM 2010.

Bladder	Urethra (prostatic urethelial carcinoma)
T4a	Tis p0 Carcinoma in situ. Involvement of prostatic urethra
T4b	Tis p0 Carcinoma in situ. Prostatic duct involvement
	T1 Tumor invading the subepithelial connective tissue
	T2 Tumor invading the prostatic stroma, corpus spongiosum, penile urethral muscle
	T3 Tumor invading the corpus cavernosum beyond the prostatic capsule, bladder neck
	T4 Tumor invading other adjacent organs (bladder)

The subepithelial invasion from the prostatic urethra is not a T4 stage.

* T4a involves prostatic stromal invasion from the bladder.

Data from Palou et al. Eur Urol. 2013;63:81-7.

Mechanisms of stromal invasion

Prostatic stromal invasion is defined by the **presence of irregular invasive tumor nests or single cells** within the dense fibromuscular stroma of the prostate or admixed within benign prostate glands.

- contiguous tumor : direct invasion of bladder tumor into the prostate as an extravesical tumor extension (stage pT3b) penetrating into the stroma directly through the prostatic capsule

- noncontiguous tumor : synchronous presence of PU tumors as a pagetoid spread of urethral tumor into the stroma via the ducts and acini

Data from Palou et al. Eur Urol. 2013;63:81-7.

Mechanisms of stromal invasion

- Several studies showed worse prognosis for contiguous versus noncontiguous growing tumors.

Table 4 - Classification of Involvement of the prostate according to Pagano et al. [37]

Stage	No. of patients (%)	Survival, %
Contiguous	44 (61)	7
Noncontiguous	28 (39)	46
Urethral mucosa	6	100
Ductal/acinar	14	50
Stromal	8	40
Extracapsular invasion	0	-



Data from Palou et al. Eur Urol. 2013;63:81-7.

Incidence of prostatic urothelial carcinoma

- Transitional cell cancer involvement of the prostate in patients with a primary bladder cancer has been reported in multiple studies with an incidence between 12% and 48%.

Table 4

Incidence of prostatic urothelial carcinoma

Superficial bladder carcinoma	16%–39%
Postcystectomy specimen	12%–48%
Postcystectomy with stromal involvement	7%–17%
Primary urothelial carcinoma of the prostate	1%–4%

Data from Walsh et al. Urol Oncol. 2009;27:352-7.

Diagnosis

- Cystoscopy was described as a valuable tool to diagnose PU involvement if there are macroscopic lesions.

- Stromal invasion detected in transurethral biopsies in the PU was reported to be **only 56%**.

Donat et al. evaluated 246 male patients undergoing cystectomy. Biopsies were obtained at the 4 and 8 o'clock positions from the bladder neck to the verumontanum. With a sensitivity of 53%, specificity of 77%, and positive predictive value of 45%, the authors concluded that transurethral biopsy is an imperfect tool for detecting.

Donat et al. J Urol. 2001;165:1580-4.

Data from Palou et al. Eur Urol. 2013;63:81-7.

Diagnosis

- To identify stromal invasion, resectoscope loop biopsies of the PU are taken from the lateral lobes and floor beginning distal to the bladder neck and extending just proximal to the verumontanum.

- The only way to approach 100% accuracy would be to perform an extensive transurethral resection of the prostate (TURP), an **impractical approach** for the routine staging of patients with bladder cancer.

- Solsona et al. recommended a prostatic biopsy in patients with **positive cytology in the absence of macroscopic tumors or CIS or in those with macroscopic lesions in the prostate.**

Data from Palou et al. Urology. 2007;69:50-61.

Predicting prostatic stromal invasion

- Given the **lack of accurate diagnostic tools**, clinical factors that might help clinicians predict stromal invasion would be particularly useful.

- Numerous articles have evaluated prognostic factors and the development of prostatic urethral involvement, but not specifically prostatic stromal invasion.

- Wood et al. identified CIS involving the trigone, bladder neck, periurethral structures, and ureter, and a history of intravesical instillations as predictors of PU involvement.

Data from Palou et al. Eur Urol. 2013;63:81-7.

Stromal invasion treatment

- Prostatic stromal invasion is associated with a higher likelihood of lymph node (LN) metastases and a poor survival.

- In patients who are surgical candidates, radical cystoprostatectomy is the treatment of choice because durable cancer control rates with radiation with or without radio-sensitizing chemotherapy are poor.

- The more extensive the dissection and the more nodes removed, the higher the staging accuracy and therapeutic benefit to patients.

Data from Palou et al. Eur Urol. 2013;63:81-7.

Follow-up of the prostatic urethra

- With increasing numbers of patients receiving initially longer courses of intravesical therapy for high-grade Ta/T1 bladder cancer or CIS rather than radical surgery, there will be an increased number of patients at risk of developing UC of the prostate.

- Solsona et al. strongly recommend frequent random biopsies of the PU during initial and repeated cystoscopic examinations.

The patients were checked quarterly in the first 2 yr and then semiannually until the fifth year.

For patients with **positive cytology in follow-up in the absence of macroscopic bladder carcinoma**, it is recommended to evaluate the bladder and the PU with multiple biopsies.

Solsona et al. Eur Urol. 1991;19:89-92.

Data from Palou et al. Eur Urol. 2013;63:81-7.

Follow-up of the prostatic urethra

- Bladder recurrence is most likely to be the cause with a positive cytology during the first 6 mo of follow-up after conservative management of a Ta/T1 bladder carcinoma.

- The PU should be considered if there has been associated **CIS, tumor near the bladder neck, or multifocal disease.**

- If positive cytology appears in longer term follow-up, the upper urinary tract should be evaluated.

Data from Palou et al. Eur Urol. 2013;63:81-7.

Conclusions

- Underreporting of the true incidence of prostatic involvement is common.

- The incidence of prostatic urothelial carcinoma in men with superficial or invasive bladder cancer ranges from 12% to 48%, and 7.6% to 16.8% have stromal invasion.

- Transurethral biopsy of the prostatic urethra is effective in identifying prostatic involvement but does not accurately reveal the extent of involvement, particularly with stromal invasion. New methods for detection of prostatic stromal invasion are needed.

- **Retrospective and prospective studies are needed to determine prognostic factors for prostatic stromal invasion.**

- Radical cystoprostatectomy is the treatment of choice for locoregional control in patients with prostatic stromal invasion.

- Data show that the extent of lymphadenectomy may have an impact on survival.

Data from Palou et al. Urology. 2007;69:50-61.

전이 신장암의 치료제로서 새로이 대두되고 있는 Pazopanib (Votrient®) 에 관한 문헌 고찰

성균관대의대 전성수

혈관형성은 고형암의 증식 및 전이에 대한 전제 조건으로 인식되므로, 항암치료의 주요 타겟이 되어왔다 (Folkman, 2003). 다양한 증식 인자 및 수용체의 상호작용을 통해 종양 혈관 신생에 영향을 주는 방식으로 작용을 하는데, 혈관내피증식인자(VEGF) axis는 확인된 가장 강력한 proangiogenic factor들이며, 중요한 치료 타겟으로 확인 되었다.

Clear cell RCC 는 높은 혈관성 종양으로, 환자의 대부분에서 VEGF, VEGFRs, 그리고 PDGFR(Gorge, 2003)의 과잉 발현이 확인 되었고 이러한 특성은 혈관형성증가, 진행성 종양 병기, 공격적 표현형, 불량한 생존과 관련이 있다(Takahashi, 1994; Jacobsen, 2000; Tsuchiya, 2001; Sulzbacher, 2003). 따라서 VEGF, VEGFR, PDGFR은 RCC 치료의 적합한 타겟이 된다. 항-혈관형성인자에 대한 연구가 발표되기 이전까지는 낮은 반응을 및 중대한 치료 관련 독성에도 불구하고, 면역 요법이 표준 치료법으로 사용되었으나(McDermott, 2004), 생존 유익성에 대한 상반되는 결과들이 보고되었다(Coppin, 2004; Negrier, 2007; Atkins, 2004; McDermott, 2004). 그러나 최근 RCC환자를 대상으로 한 Tyrosine kinase inhibitor을 포함한 표적치료제의 개발로 인해 질병의 무진행 생존기간 (PFS) 이 11개월을 넘는 등 유망한 결과가 보고 되고 있다 (Motzer, 2006; Escudier, 2007; Sternberg, 2010).

그러나 이러한 치료효과의 개선에도 불구하고, TKI와 연관된 부작용 (피로, 수족증후군, 구내염 등)으로 인해 TKI 치료를 받는 RCC환자의 삶의 질에 대한 불만족은 RCC 치료의 미제로 남아 있었다. (Hutson et al. Oncologist 2008;13:1084-96.; Porta and Szczylik. Cancer Treat Rev 2009;35:297-307.)

파조파닙은 VEGFR, PDGFR, c-Kit을 표적으로 하는 경구 혈관형성 저해제로, 다양한 종양의 치료제로써 임상 개발 중에 있으며 진행성 신세포암종의 1차 이상 치료제와 이전 화학 요법을 투여 받은 진행성 연조직육종 치료제로 허가 및 급여를 인정 받았다. 진행성 신세포암에서 파조파닙의 주요 제 3상 연구인 VEG105192에서는 ECOG performance status가 0 또는 1이면서 이전에 치료를 받은 적이 없는 환자 233명과 사이토카인 치료를 받은 환자 202명을 대상으로 하였고, 질환이 진행된 후 교차가 허용되었기 때문에, 1차 평가변수는 무진행 생존(PFS)로 하였다. 이전 치료 경험이 없는 환자군 중 파조파닙을 투약받은 군의 PFS중간값은 11.1개월로 대조군의 2.8개월과 비교하여 위험비(HR) 0.40(95% CI 0.27 to 0.60, $p < 0.001$)으로 나타났다. 이전에 사이토카인 치료에 실패한 소그룹에서, PFS의 중앙값은 파조파닙 투약군과 위약군에서 각각 7.4개월 및 4.2개월이었고, 위험율은 0.54 (95% CI: 0.35 to 0.84, $p < 0.001$) 였다. 모든 소그룹의 분석은 독립적 심의 위원회 (IRC)평가에 근거하였다.

파조파닙 투약한 피험자에서 가장 흔한 약물관련 이상반응은 설사 (44%), 고혈압 (37%), 그리고 모발 변색 (37%)이었다. 하지만, 설사와 고혈압의 중대한 이상반응 발생율은 4% 미만으로 낮았다. 투여 후 발생한 설사 및 고혈압의 대부분은 표준치료법으로 조절할 수 있었고, 이를 통해 피험자가 시험약 투여를 계속할 수 있었다. 가장 흔한 Grade 3, 4의 실험실 이상은 ALT 및 AST의 상승이었고(피험자의 3.4%에서 시험약 중단), 약물-관련 간 효소 상승 또는 기능적 이상의 대부분은 투약 용량 조절을 통해 회복되었다. 백혈구 감소증, 호중구 감소증 및 혈소판 감소증등의 혈액학적 부작용은 위약군에 비해 파조파닙 투약군에서 더 흔하였으나, Grade 3,4의 혈구 감소증은 5% 미만으로 흔하지 않았다. 이 부분은 in vitro data결과를 통해 설명이 가능한데, 파조파닙은 in vitro data에서 혈액학적부작용과 연관되어 있는 Flt-3를 수니티닙에 비해 350배 정도 덜 저해하는 것으로 보고 되었다 (Kumar et al. Br J Cancer 2009; 101: 1717-1723).

이 3상 임상연구에서는 양군의 HRQoL도 2차 평가변수 중 하나로 평가 되었는데, 임상연구 진행기간 동안 양군 간 QoL에는 차이가 없음을 보이며 파조파닙이 환자의 QoL을 유지시켜 주었다.

결론적으로 파조파닙은 투명세포성 진행성신세포암의 1차 또는 이전에 싸이토카인 치료에 실패한 2차 치료에 효과적인 치료제라고 말할 수 있다.

오스트리아 비엔나에서 개최된 12차 ESMO 심포지움에서 발표된 COMPARZ(COMPARing the efficacy, sAFety and toleRability of paZopanib vs. sunitinib) 임상의 책임 연구자인 Robert J. Motzer(미국 메모리얼 슬로언 캐터링 암센터) 박사의 발표에 따르면, 파조파닙이 질병 무진행 생존기간(PFS) 직접 비교 임상에서 결과적으로 수니티닙과 유사한 것으로 나타났으며, 삶의 질 평가를 위한 14개 항목 중에서 11개 항목에서 파조파닙 투약군에 통계적으로 유의하게 우호적으로 나왔다. COMPARZ임상은 이전에 치료 경험이 없는 진행성/전이성 신세포암 환자 1110명을 대상으로 파조파닙과 수니티닙 군으로 무작위 배정되었다. 이 연구의 일차 결과 변수는 질병 무진행 생존기간(PFS)이었고, 이차 결과 변수는 전체 생존기간(OS), 객관적 반응률(ORR), 안전성(Safety profile), 그리고 삶의 질(HRQoL) 평가 등 이었다. COMPARZ 임상에서 파조파닙과 수니티닙의 비 열등성을 입증하기위해 선결정된 범주는 1.25(양측상위한도95% CI)였다.

독립적 심의 위원회 (IRC)의 평가에 따르면 파조파닙군의 질병 무진행 생존기간 중앙값은 8.4개월(95% CI 8.3 to 10.9), 수니티닙은 9.5개월(95% CI 8.3 to 11.1) 로 HR 1.05이었고, 연구자 평가에 따른 양 군의 무진행 생존기간 중앙값은 파조파닙 10.5개월 (95% CI 8.3 to 11.1), 수니티닙10.2개월 (95% CI 8.3 to 11.1) 로 HR0.908이었으며, 객관적 반응률(ORR)은 각각 31%, 25% (p=0.032)였다. 전체생존기간 중앙값은 각각 28.4개월(95% CI 26.2 to 35.6), 29.3개월(95% CI 25.3 to 32.5)였고, 양군의 위험비(Hazard Ratio)는 0.908(95% CI 0.762 to 1.082,p=0.275)였다. 따라서, 질병 무진행 생존기간은 물론, 객관적 반응률이나 전체 생존기간 등에서 큰 차이를 보이지 않아 비열등성이 입증되었다.

이 연구에서 파조파닙 투약 환자 중 3%이상에서 발생한 중대한 이상반응은 AST와 ALT 수치의 증가였고, 수니티닙 투약 환자 중 3%이상에서 발생한 중대한 이상반응은 발열과 혈소판 감소였고 치료 중 발생하는 수족증후군, 구내/인후 쓰림, 피로감등을 통해 삶의 질을 평가하기 위한 14개 지표 중 11개의 지표가 통계적으로 유의하게 파조파닙 투약군에 우호적으로 나타났다.

또한, PISCES study를 통하여 환자와 임상의의 파조파닙과 수니티닙에 대한 선호도가 평가된 바 있다. 이 연구는 각각의 약제를 10주씩 투약 받은 뒤 두 약제 중 더 선호하는 약제를 환자가 직접 선택해 이 후 지속적으로 투약하도록 이중맹검으로 디자인되었다. 이 연구의 일차결과변수인 환자들의 선호도에 따르면, 파조파닙을 선호한다는 응답은 70%, 수니티닙을 선호한다는 응답은 22%였고, 임상의들을 대상으로 한 선호도 조사에서도 각각 61%, 22%로 조사되었다. 선호도에 대한 이유를 조사한 항목에서 대부분의 환자들이 전반적으로 더 나은 삶의 질, 수족증후군의 적음, 적은 피로도 등 여러가지 이유로 파조파닙에 선호도를 나타내었다고 조사되었다.

이들 연구결과는 가장 적절하고 효과적인 TKI 치료의 방법에 대한 직접비교 정보를 제공함으로써 임상의의 치료 약제 선택에 도움을 줄 수 있을 것으로 기대된다. 이를 바탕으로 투명세포성 진행성 신세포암에서 기존 치료제인 수니티닙과 효과적으로 유사하며 차별화된 이상반응 프로파일을 통해 치료 기간 중 더 나은 삶의 질을 제공할 수 있는 파조파닙은 이 환자군에서 고려되어야 할 중요한 치료옵션이라 할 수 있다.

Q 공지사항



● 대한비뇨기종양학회-대한내비뇨기과학회 공동 심포지엄

2013년 9월 28일(토), 대전 을지대학병원

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- 공모 지원 자격: 대한비뇨기종양학회 회원

- 공모논문 대상 및 우수상: 7월말까지 완성된 논문을 작성하시어 학회로 제출해주시면, 이 가운데 대상 및 우수상을 각각 1편씩 선정하여, 대상 200만원, 우수상 100만원을 지원할 예정입니다.

선정된 논문은 추후 대한비뇨기종양학술지에 게재됨을 알려드립니다.

(타학술지와 이중 게재 금지)

- 제출서류: 논문 완성본 한글 또는 워드 파일로 메일접수

- 보내실곳: 학술위원회 위원장 조진선 교수

- 제출기한: 2013년 7월 31일

- 제출한 논문은 학술위원회에서 심사하여 2013년 추계학술대회에서 시상할 예정입니다.

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2013년도 대한비뇨기종양학회 연구과제를 대한비뇨기종양학회 연구위원회 규정에 따라 공모합니다.

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3. 2013년 7월 31일까지 연구위원회에 이메일로 접수시켜 주시기 바랍니다.

연락처에 명시된 이메일에 접수하여 주시고, 접수되었다는 답신을 확인 부탁드립니다.

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4. 2008년 9월 1일부터 시행되고 있는 대한비뇨기종양학회 연구위원회 규정 및 시행세칙을 참조하고 준수하시기 바랍니다.

[문의처]

연구위원장 변석수 교수

PFS: Progression Free Survival

+
3/4등급 이상반응의
낮은 발생률

Votrient® pazopanib

[illegible]

Ref. Sternberg CN, *et al.* Pazopanib in locally advanced and/or metastatic renal cell carcinoma: result of a randomized phase III trial. *J Clin Oncol* 2010;28:1061-8

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