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Genitourinary Oncology Update 2021

Matthew Milowsky MD

April 28, 2021

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Disclosures

- Employment - none
- Leadership - none
- Stock and Other Ownership Interests – none
- Honoraria - none
- Consulting or Advisory Role – none
- Speaker's Bureau - none
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- Patents, Royalties, Other Intellectual Property – none
- Expert Testimony - none
- Travel, Accommodations, Expenses - none
- Other Relationship - none

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2021 GU Cancers Symposium Highlights

ADC, radioligand therapy, adjuvant immunotherapy,

Lu-177-PSMA therapy for prostate cancer

Adjuvant Nivolumab in MUC

Enfortumab Vedotin for advanced urothelial cancer

and more...

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Prostate Cancer Update

1. TheraP (ANZUP 1603) – Lu-177-PSMA in mCRPC
2. ACIS – Apa/Abi vs. Abi in mCRPC



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TheraP (ANZUP 1603)

¹⁷⁷Lu-PSMA-617 (LuPSMA) versus cabazitaxel in metastatic castration resistant prostate cancer (mCRPC) progressing after docetaxel: updated results including progression free survival (PFS) and patient-reported outcomes (PROs)

TheraP (ANZUP 1603)

Michael Holman, Louise Emmett, Shaheen Sandhu, Amir Iravani, Anthony Joshua, Jeffrey Goh, David Petropoulos, Huang Tan, Ian Kirkwood, Sothun Ng, Roslyn Francis, Craig Godfrey, Natalie Rutherford, Alison Zhang, Margaret McInnert, Martin Stockler, John Valler, Scott Williams, Andrew Martin, Ian Davis on behalf of the TheraP Investigators

TheraP is a partnership between ANZUP Cancer Trials Group and the Prostate Cancer Foundation of Australia (PCFA) in collaboration with the NIMRC CTC and the Australasian Radio-pharmaceutical Trials Network (ARTN) with support from the Australian Nuclear Science and Technology Organisation (ANSTO) and Endocyte Inc., a Novartis company

<https://doi.org/10.1093/annonc/mdz408>

Contributory Cancer Symposium

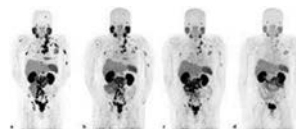
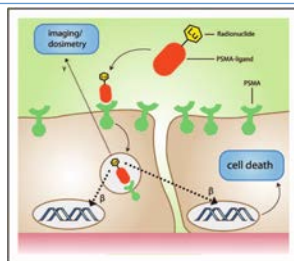
Presented by: Michael Holman

ANZUP Cancer Trials Group

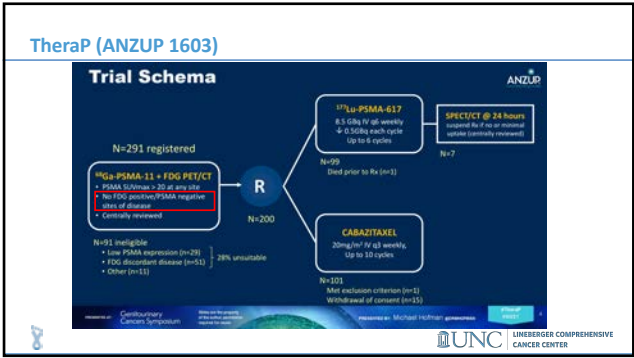


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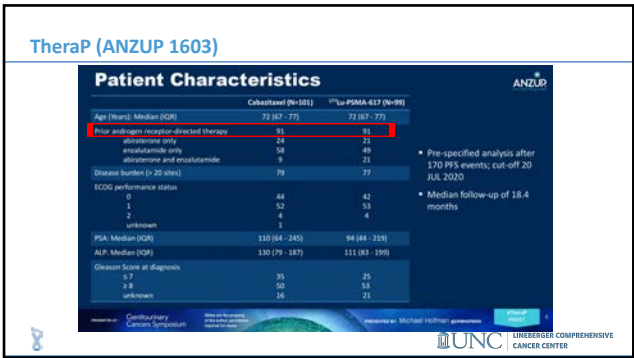
177-Lu-PSMA-617



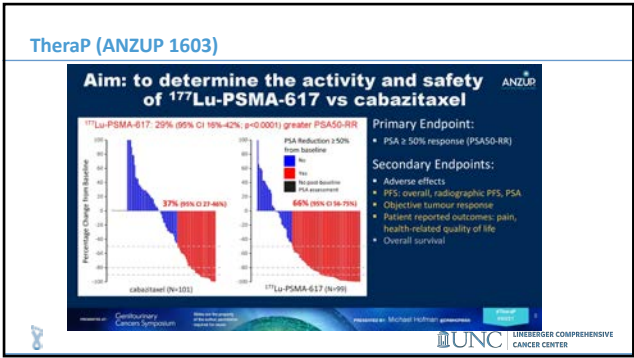
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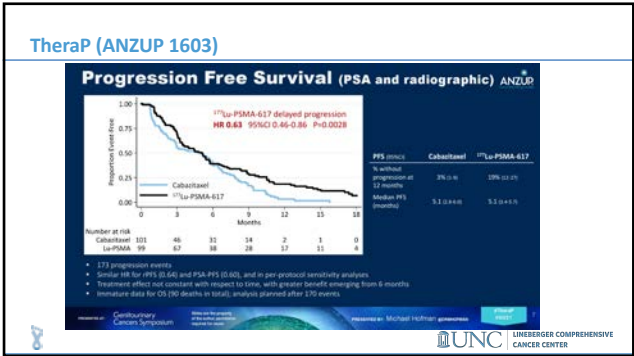
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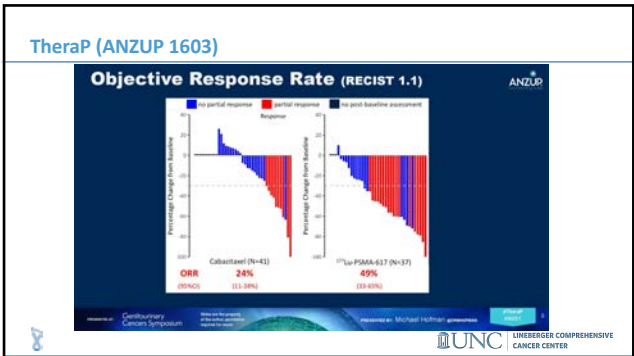
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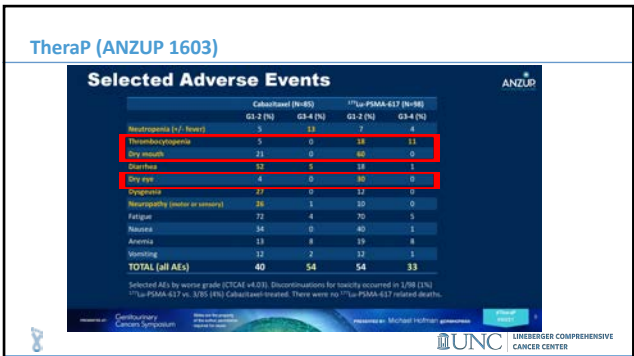
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Press Release (3/23/2021): Phase III VISION study

Novartis announces positive result of phase III study with radioligand therapy ¹⁷⁷Lu-PSMA-617 in patients with advanced prostate cancer

- Phase III VISION study with ¹⁷⁷Lu-PSMA-617 met both primary endpoints, significantly improving overall survival (OS) and radiographic progression-free survival (rPFS) in patients with PSMA-positive metastatic castration-resistant prostate cancer¹

Likely practice changing (awaiting data)

<https://www.novartis.com/news/media-releases/novartis-announces-positive-result-phase-iii-study-radioligand-therapy-177lu-psma-617-patients-advanced-prostate-cancer>

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ACIS

Abstract #9

Results From ACIS, a Randomized, Placebo-Controlled Double-Blind Phase 3 Study of Apalutamide and Abiraterone Acetate Plus Prednisone Versus Abiraterone in Patients With Chemo-Naïve Metastatic Castration-Resistant Prostate Cancer

Dana E. Rathkopf,¹ Eleni Eleftheriou,² Gerhardt Attard,³ Thomas W. Flaig,⁴ Fabio Andre Franke,⁵ Oscar B. Goodman Jr.,⁶ Stéphane Oudard,⁷ Thomas Stauber,⁸ Hiroyoshi Suzuki,⁹ Diaphne Wu,¹⁰ Kesar Yanuva,¹¹ Peter De Porne,¹¹ Sabine Brookman-May,^{12,13} Susan Li,¹³ Jinhui Li,¹⁴ Suneel Mundie,¹⁵ Sharon A. McCarthy,¹⁶ Fred Saad,¹⁷ on behalf of the ACIS Investigators

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ACIS

ACIS Study Schema: Randomized, Placebo-Controlled Double-Blind Phase 3 Study^a

Patients
N = 812

Inclusion Criteria:
• mCRPC progression on ADT
• ECOG PS 0 or 1
• Pain score (BPI-SF) ≤ 3
• No prior chemo or ABI for castration-resistant disease

Stratification Factors:
• Presence or absence of visceral metastases
• ECOG PS 0 or 1
• Geographic region (North America, Europe/UK or rest of world)

Randomized
1:1

APA (APA 1000mg QD + AAR 1000mg QD) + P
28-day treatment cycles until disease progression, withdrawal of consent, or occurrence of unacceptable toxicity. Patients treated ongoing QOL.

Placebo + AAR
(AAR 1000mg QD) + P (P 10mg QD)

Primary End Point
• mPFS (by investigator)

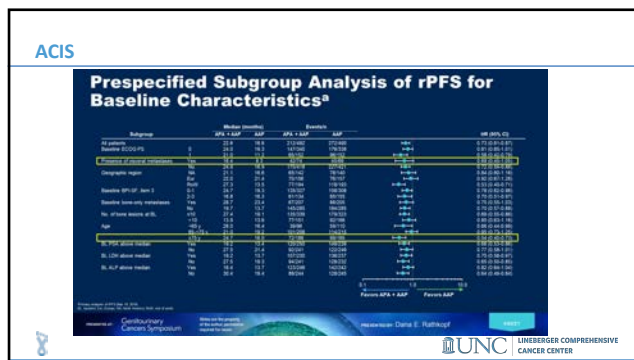
Secondary End Points
• Overall survival (OS)
• Time to initiation of cytotoxic chemotherapy
• Time to pain progression
• Time to chronic opioid use

Exploratory End Points
• Time to clinical progression
• Time to first subsequent anticancer therapy
• Time to second progression-free survival
• Decline in PSA level
• Time to PSA progression
• Prospective subgroup analysis by patient characteristics and tumor signatures
• Patient-reported outcomes (ACIP-P)
• Safety

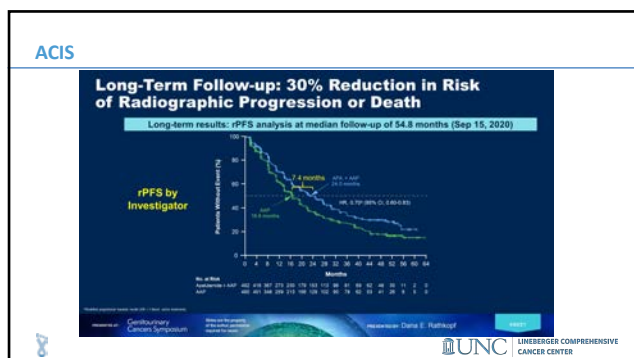
Long-term follow-up every 3 months

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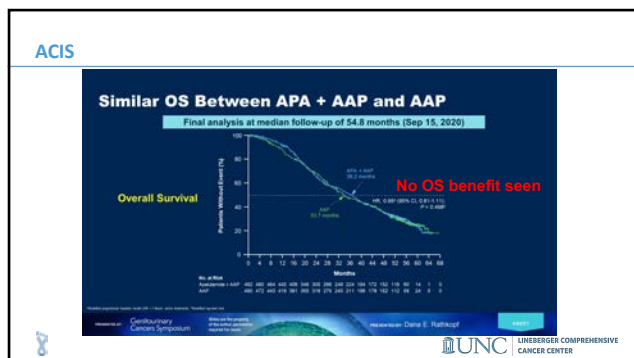
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ACIS – Not practice changing without improvement in OS

ACIS Conclusions

- ACIS met its primary end point of rPFS, as assessed by investigator, in chemotherapy-naïve mCRPC
- rPFS was extended by 6 months in primary per-protocol analysis and by 7.4 months in the updated final analysis with APA + AAP versus AAP ($P < 0.0001$)
- The rPFS benefit was observed versus AAP, an active comparator
- Secondary end points, including OS, were similar between arms
- No new safety signals were observed
- Slightly higher rates of TEAEs were seen with APA + AAP; however, the quality of life was comparable between treatment arms (FACT-P Total)
- Clinical/biomarker subgroups of patients may derive greater benefit with APA + AAP

Investigator: Genitourinary Cancer Symposium | Date: 10/10/2018 | Slide: 20/20 | © 2018 ASCO

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Bladder Cancer Update

1. EV-301– EV vs. Chemotherapy in mUC (previously treated)
2. EV-201 – EV in cisplatin-unfit mUC (prior IO)
3. CheckMate 274 – adjuvant Nivolumab in high-risk MIUC

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EV-301

**Primary Results of EV-301:
A Phase 3 Trial of Enfortumab Vedotin vs
Chemotherapy in Patients With Previously
Treated Locally Advanced or Metastatic
Urothelial Carcinoma**

Thomas Powles, MD^{1*}, Jonathan E Rosenberg, MD^{2*}, Guru P Sonpavde, MD³,
Yohann Loriot, MD, PhD⁴, Ignacio Durán, MD, PhD⁵, Jae-Lyun Lee, MD, PhD⁶,
Nobuaki Matsubara, MD⁷, Christof Vultsteke, MD, PhD⁸, Chunzhang Wu, PhD⁹,
Mary Campbell, MD¹⁰, Maria Matsugou, MBChB, MD¹¹, Daniel P Petrylak, MD¹¹

¹North Central Cancer Center, Queen Mary University of London, London, United Kingdom; ²Memorial Sloan-Kettering Cancer Center, New York City, NY, USA; ³Carroll Feller Cancer Institute, Harvard Medical School, Boston, MA, USA; ⁴Hospices de France, Université Paris-Saclay, Villejuif, France; ⁵Hospital Universitario Marqués de Valdecilla, IDIVAL, Cantabria, Spain; ⁶Yonsei Medical Center and University of Seoul College of Medicine, Seoul, South Korea; ⁷National Cancer Center Hospital East, Chiba, Japan; ⁸Center for Oncological Research (CORE), University of Antwerp, Integrated Cancer Center Ghent, Ghent, Belgium; ⁹Novartis Pharma Inc., Northbrook, IL, USA; ¹⁰Novartis Inc., Redwood City, CA, USA; ¹¹Temple Cancer Center, Yale School of Medicine, New Haven, CT, USA

*Chair and co-authorship Drs. Powles and Rosenberg contributed equally to this presentation

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EV-301

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Enfortumab Vedotin

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Enfortumab Vedotin

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EV-301

EV-301 Open-Label Phase 3 Trial Design

Key eligibility criteria:

- Histologically confirmed locally advanced or metastatic urothelial carcinoma with progression after first-line treatment
- Performance status of 0-1
- ECOG PS 0 or 1

Enfortumab vedotin (N=381)

- 1.0 mg/kg
- IV over 30 min
- Q2W for 12 cycles

Primary endpoint: Overall survival

Secondary endpoints:

- Progression-free survival
- Disease control rate
- Overall response rate
- Safety

Investigator assessment per RECIST v1.1

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EV-301

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Progression-free Survival



Investigator-Assessed Overall Response



Treatment-Related Adverse Events

0

EV-301 – Practice changing

EV-301: Conclusions

Efficacy

Enfortumab vedotin had superior overall survival compared with chemotherapy in patients with advanced UC who had previously received platinum-based chemotherapy and a PD-L1 inhibitor

- Enfortumab vedotin showed superior progression-free survival and response rates compared with chemotherapy
- Subgroup analyses also broadly showed benefit in the enfortumab vedotin arm
- Results were consistent with phase 1 and 2 studies

Safety

Enfortumab vedotin demonstrated a tolerable and manageable safety profile

- No new safety signals were identified; safety profile was consistent with prior enfortumab vedotin studies
- Adverse events of special interest (eg, skin reactions, peripheral neuropathy, and hypothyroidism) were generally mild/moderate in severity and consistent with those reported in prior studies

Overall

Enfortumab vedotin is the first drug, beyond chemotherapy and immunotherapy, to show significant survival advantage in previously treated advanced UC

Continuity Cancer Symposium

What's the practice change?

Enfortumab Vedotin

Presented by: Thomas Pisters

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EV-201

EV-201 Cohort 2: Enfortumab vedotin in cisplatin-ineligible patients with locally advanced or metastatic urothelial cancer who received prior PD-1/PD-L1 inhibitors (NCT03219333)

Arjun V. Balar, Bradley McGregor, Jonathan Rosenberg, Michiel S. van der Heijden, Se Hoon Park, Jae Lyn Lee, Michael R. Harrison, Elisabeth I. Heath, Mark N. Stein, Yohann Loriot, Andrea Necchi, Joyce Steinberg, Shang-Ying Liang, Eric Kim, Janet Trowbridge, Mary Campbell, Daniel P. Petrylak, and Evan Y. Yu

Continuity Cancer Symposium

What's the practice change?

Enfortumab Vedotin

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EV-201

EV-201: Non-Comparative, Pivotal Phase 2 Trial

Enrollment: 59 Global Sites

Previously treated locally advanced or metastatic urothelial carcinoma

Target Enrollment: ~100 patients/cohort

Cohort 1

Prior PD-L1/PD-L1 inhibitor and platinum-based therapy

Enrollment Completed: July 2018 (N=27)

Cohort 2

Prior PD-1/PD-L1 inhibitor, platinum-naïve (platinum ineligible)

Enrollment Completed: February 2020 (N=32)

Enfortumab vedotin

1.25 mg/kg IV on days 1, 8, and 15 of each 28-day cycle

Primary endpoint: Confirmed ORR as determined by BCR

Other endpoints: OS, DFS, PFS, QoL

Safety & Toxicity

Continuity Cancer Symposium

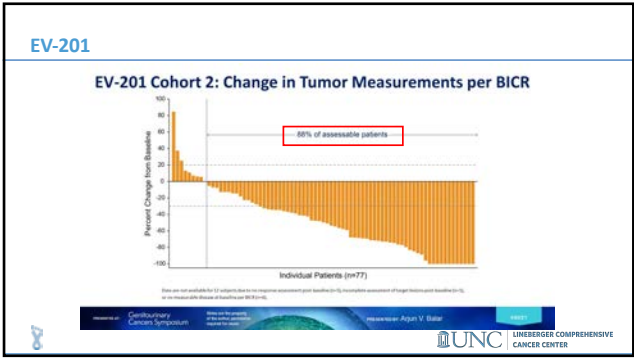
What's the practice change?

Enfortumab Vedotin

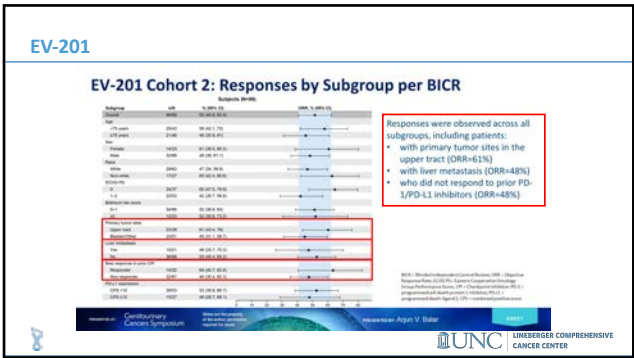
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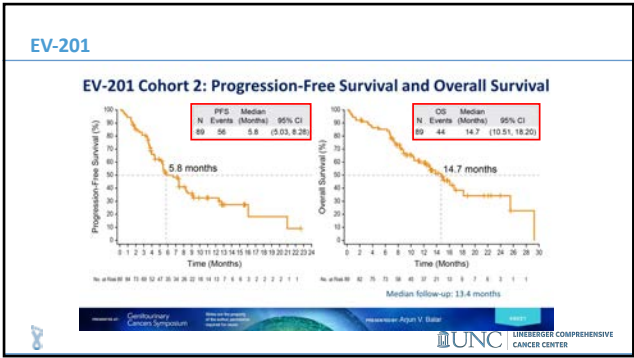
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EV-201 – Promising but not practice changing at this time

EV-201 Cohort 2: Summary and Conclusions

- Following immunotherapy, cisplatin-ineligible patients need effective treatment options
- The response rates to EV in this study are numerically the highest observed for any regimen in cisplatin-ineligible patients with advanced urothelial carcinoma
 - 52% ORR, with 20% CR rate
 - 10.9 months median duration of response
 - Response rates were consistent across all subgroups
- Tolerable safety profile in an elderly patient population ineligible for cisplatin
- Activity demonstrated in EV-201 Cohort 2 builds upon the overall survival benefit shown in PD-1/PD-L1 inhibitor and platinum-treated patients in EV-301
- These data support continued investigation of EV across the spectrum of urothelial carcinoma and may support a new standard of care for this population with unmet need

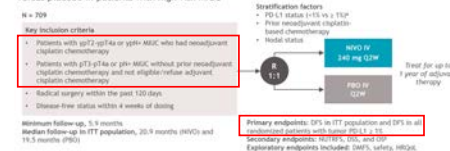
EV-201 Cohort 2: Summary and Conclusions

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CheckMate 274

Study design

- CheckMate 274 is a phase 3, randomized, double-blind, multicenter study of adjuvant nivolumab versus placebo in patients with high-risk AUC



Minimum follow-up: 5.9 months
Median follow-up in ITT population: 20.9 months (NIVO) and 19.5 months (PBO)

Statistical design

Two primary objectives

- To compare DFS for NIVO versus PBO in all randomized patients (ITT)
- To compare DFS for NIVO versus PBO in all randomized patients with PD-L1 ≥ 1%

Sample size calculation (~700 patients)

Power considerations

Interim analysis

Adjusted alpha level at interim analysis

Key secondary objective

OS (secondary endpoint) to be tested using hierarchical procedure in each population, per the statistical analysis plan

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CheckMate 274

Statistical design

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CheckMate 274

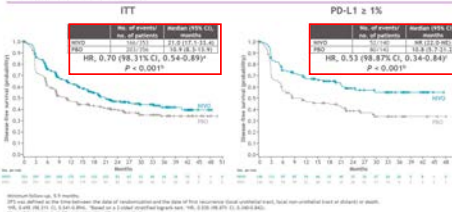
Select baseline demographic and disease characteristics in all randomized patients

	ITT N=274	PD-L1 N=274
Age, years	62.4 (SD 10.0)	62.3 (SD 10.0)
Region, %		
United States	13.9	14.9
Europe	48.2	48.8
Asia	22.7	22.8
Rest of world	15.2	13.5
ECOG PS, %		
0	43.8	42.7
1	56.2	57.3
≥ 2	0.0	0.0
Number of prior diagnoses, %		
0	79.2	79.1
1	20.8	20.9
≥ 2	0.0	0.0
ECOG PS ≥ 1 in prior diagnosis, %		
0	67.1	68.3
1	32.9	31.7
≥ 2	0.0	0.0
Number of prior diagnoses, %		
0	79.2	79.1
1	20.8	20.9
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CheckMate 274

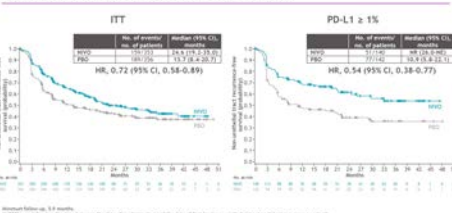
Disease-free survival



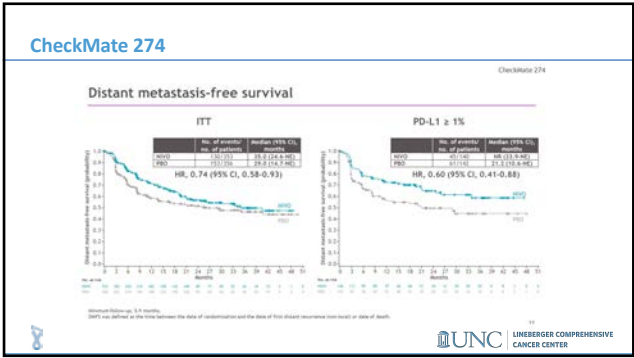
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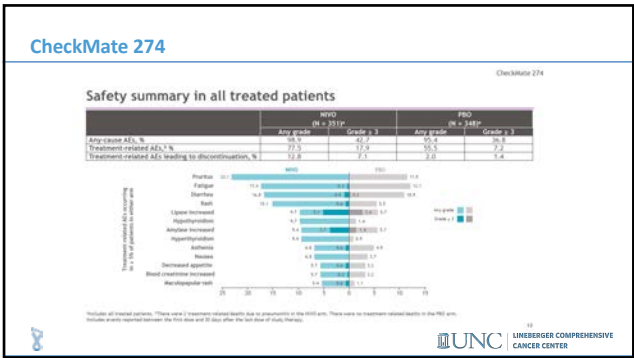
Non-urothelial tract recurrence-free survival



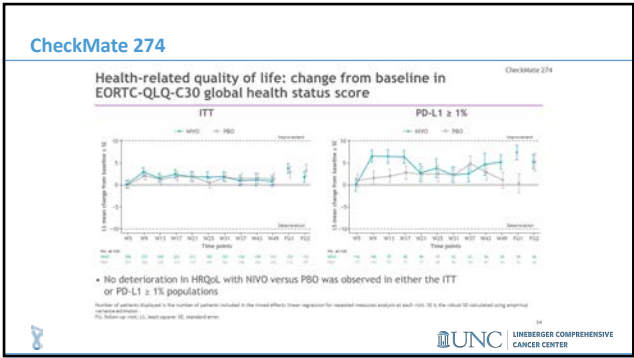
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CheckMate 274 – Potential to be practice changing...

Summary

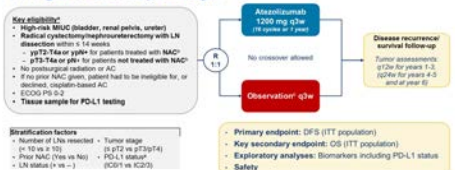
- Adjuvant NIVO significantly improved DFS in patients with high-risk MIUC after radical surgery, both in the ITT and PD-L1 $\geq 1\%$ populations
- NUTRF5 (secondary endpoint) and DMFS (exploratory endpoint) were also improved with NIVO versus PBO in both study populations
- The safety and tolerability of NIVO monotherapy was consistent with previous reports in other tumor types, including in patients with metastatic UC¹⁻³
- No deterioration in HRQoL, as measured by change in EORTC QLQ-C30 global health status score, was observed with NIVO versus PBO
- NIVO is the first systemic immunotherapy to demonstrate a statistically significant and clinically meaningful improvement in outcomes when administered as adjuvant therapy to patients with MIUC^{4,5}
- These results support NIVO monotherapy as a new standard of care in the adjuvant setting for patients with high-risk MIUC after radical surgery, regardless of PD-L1 status and prior neoadjuvant chemotherapy

Reported at: American Society of Clinical Oncology (ASCO) Annual Meeting 2019, June 1-5, 2019, San Francisco, CA. Abstract 450P. J Clin Oncol 37:450P (2019). DOI: 10.1200/JCO.2019.37.450P. © 2019 by American Society of Clinical Oncology. All rights reserved.

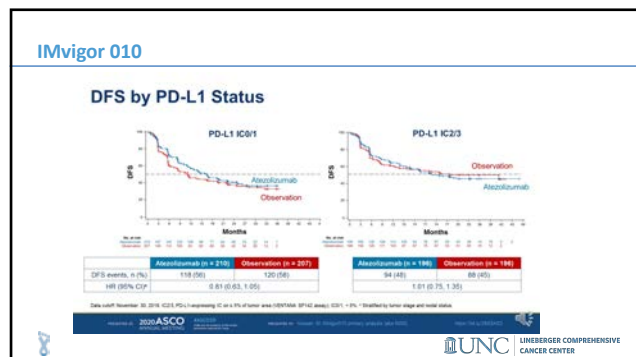
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IMvigor 010

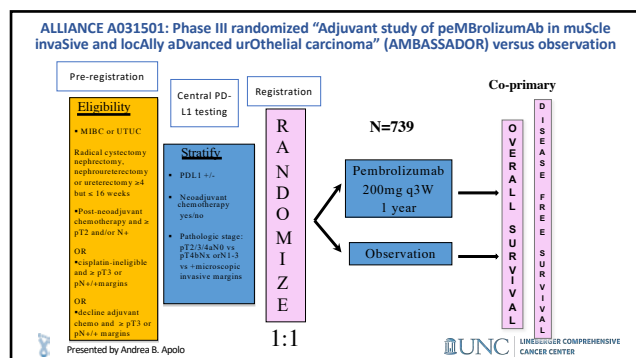
IMvigor010 Study Design



AC, adjuvant chemotherapy; DFS, disease-free survival; ITT, intention to treat; LN, lymph node; MIUC, muscle-invasive UC; NAC, neoadjuvant chemotherapy; NUTRF5, neutrophil-to-lymphocyte ratio; OS, overall survival; PD-L1, programmed death-1; pT, pathologic tumor stage; pT3-T4a, pT3-T4a or pT4b; pT4b, pT4b or pT4c; pT4c, pT4c or pT4d; pT4d, pT4d or pT4e; pT4e, pT4e or pT4f; pT4f, pT4f or pT4g; pT4g, pT4g or pT4h; pT4h, pT4h or pT4i; pT4i, pT4i or pT4j; pT4j, pT4j or pT4k; pT4k, pT4k or pT4l; pT4l, pT4l or pT4m; pT4m, pT4m or pT4n; pT4n, pT4n or pT4o; pT4o, pT4o or pT4p; pT4p, pT4p or pT4q; pT4q, pT4q or pT4r; pT4r, pT4r or pT4s; pT4s, pT4s or pT4t; pT4t, pT4t or pT4u; pT4u, pT4u or pT4v; pT4v, pT4v or pT4w; pT4w, pT4w or pT4x; pT4x, pT4x or pT4y; pT4y, pT4y or pT4z; pT4z, pT4z or pT4aa; pT4aa, pT4aa or pT4ab; pT4ab, pT4ab or pT4ac; pT4ac, pT4ac or pT4ad; pT4ad, pT4ad or pT4ae; pT4ae, pT4ae or pT4af; pT4af, pT4af or pT4ag; pT4ag, pT4ag or pT4ah; pT4ah, pT4ah or pT4ai; pT4ai, pT4ai or pT4aj; 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Kidney Cancer Update

1. CLEAR – Len/Pem in advanced ccRCC
2. SWOG 1500 – Cabo in pRCC

Presented by Andrea B. Apolo

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CLEAR

Phase 3 trial of lenvatinib plus pembrolizumab or everolimus versus sunitinib monotherapy as a first-line treatment for patients with advanced renal cell carcinoma (CLEAR study)

Robert Motzer¹, Camillo Porta², Masatoshi Eto³, Thomas Powles⁴, Viktor Grünwald⁵, Thomas E. Hutson⁶, Boris Alekseev⁷, Sun Young Rha⁸, Evgeny Kopylov⁹, Maria José Mander Vidas¹⁰, Sung-Hoi Hong¹¹, Anil Kapoor¹², Teresa Alonso Gordoa¹³, Jeffrey C. Goh¹⁴, Jaime B. Marchioni¹⁵, Alan S. Smith¹⁶, Kari Mody¹⁷, Rodolfo A. Perez¹⁸, Dongquan Yang¹⁹, and Tom K. Choueiri²⁰

¹Memorial Sloan-Kettering Cancer Center, New York, NY, USA; ²San Mateo University Hospital/Universidad Peru, Peru; ³Keio University, Yokohama, Japan; ⁴The Royal Free NHS Trust, London, England, UK; ⁵University Hospital Bonn, Bonn, Germany; ⁶Yonsei University College of Medicine, Seoul, Korea; ⁷University of Medicine and Health Sciences, Bangladesh; ⁸Seoul National University, Seoul, South Korea; ⁹Yonsei University College of Medicine, Seoul, South Korea; ¹⁰University of Medicine and Health Sciences, Bangladesh; ¹¹Yonsei University College of Medicine, Seoul, South Korea; ¹²University of Medicine and Health Sciences, Bangladesh; ¹³University of Medicine and Health Sciences, Bangladesh; ¹⁴University of Medicine and Health Sciences, Bangladesh; ¹⁵University of Medicine and Health Sciences, Bangladesh; ¹⁶University of Medicine and Health Sciences, Bangladesh; ¹⁷University of Medicine and Health Sciences, Bangladesh; ¹⁸University of Medicine and Health Sciences, Bangladesh; ¹⁹University of Medicine and Health Sciences, Bangladesh; ²⁰University of Medicine and Health Sciences, Bangladesh

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CLEAR

Study Design

Key eligibility criteria

- Advanced clear-cell RCC
- Treatment naïve
- Performance status ≥ 0
- Measurable disease
- Adequate organ function

Stratification factors

- Geographic region: Western Europe and North America vs Rest of the World
- MSKCC risk category: Favorable, Intermediate, or Poor

R (1:1:1)

Arms:

- LENV + PEM:** Lenvatinib 20 mg oral QD + Pembrolizumab 350 mg IV Q3W
- LENV + EVE:** Lenvatinib 20 mg oral QD + Everolimus 10 mg oral QD
- SUN:** Sunitinib 50 mg oral QD 4 weeks on / 2 weeks off

Primary endpoint: PFS by RECIST v1.1

Secondary endpoints: OS, ORR by RECIST v1.1, Safety, HRQoL

Key exploratory endpoints: DOR, Biomarkers

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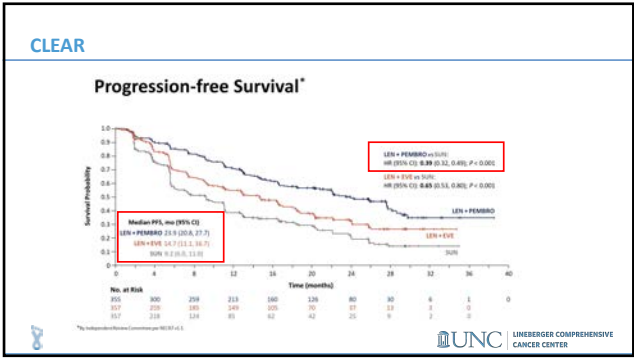
CLEAR

Baseline Characteristics

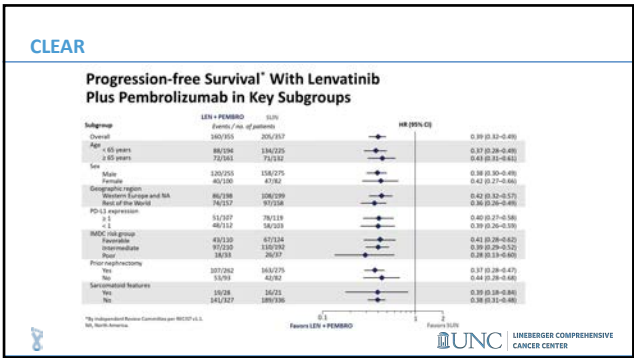
	LEN + PEM (n = 355)	LEN + EVE (n = 357)	SUN (n = 357)
Median age (range) — years	64 (34–88)	62 (32–86)	61 (29–82)
Geographic region — %			
Western Europe and North America	55.8	56.0	55.7
Rest of the World	44.2	44.0	44.3
MSKCC prognostic risk group — %			
Favorable / Intermediate / Poor	27.0 / 63.9 / 9.0	27.5 / 63.6 / 9.0	27.2 / 63.9 / 9.0
MDC risk group — %			
Favorable / Intermediate / Poor	31.0 / 59.2 / 9.3	31.9 / 54.6 / 11.8	34.7 / 53.8 / 10.8
Sarcomatoid features — %	7.9	6.7	5.9
PD-L1 expression — %			
≥ 1 / < 1 / not available	30.1 / 31.5 / 38.3	32.5 / 33.1 / 34.5	33.3 / 28.9 / 37.8
Prior nephrectomy — %	73.8	72.8	77.0

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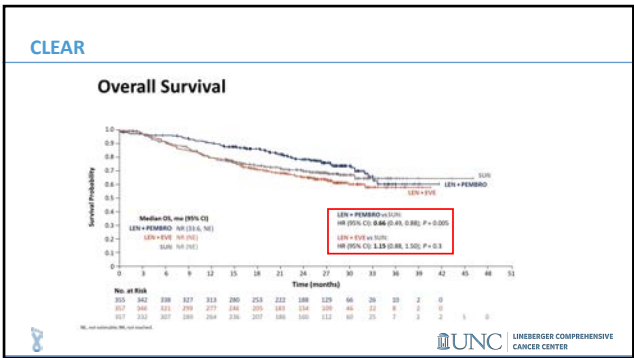
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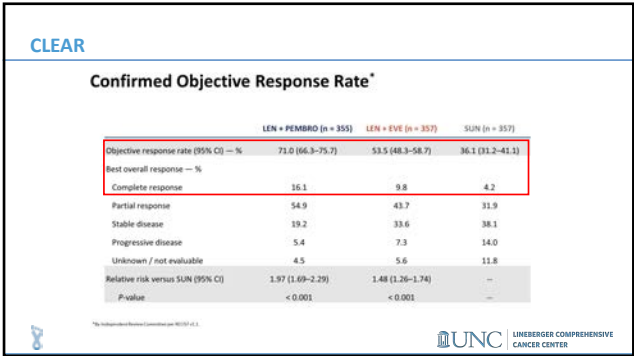
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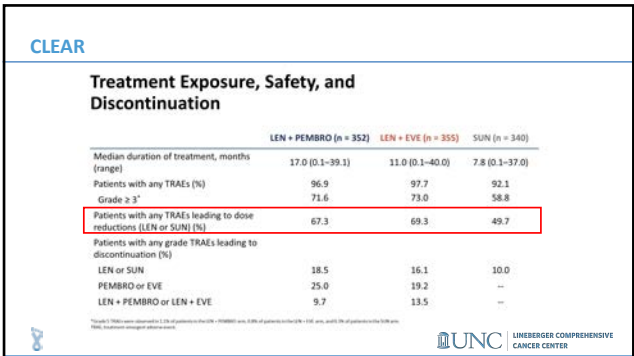
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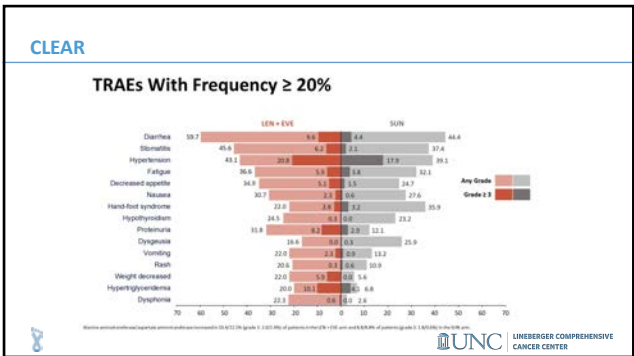
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CLEAR – Practice changing as another IO/VEGFR TKI combo

Conclusions

- Lenvatinib plus pembrolizumab demonstrated significant improvements in PFS, OS, and ORR versus sunitinib
- Lenvatinib plus everolimus demonstrated significant improvements in PFS and ORR but not OS versus sunitinib
- The safety profiles of lenvatinib plus pembrolizumab and lenvatinib plus everolimus were consistent with each drug's known profile and manageable, as needed, through dose modifications
- These results support lenvatinib plus pembrolizumab as a potential first-line treatment for patients with advanced RCC



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First-line options for metastatic ccRCC

	Checkmate 214 (Int/Poor)	Keynote 026 (Poor/Abs)	Checkmate 9ER (Nivo/Cabo)	CLEAR (Pem/Lenva)
IMDC Fav/Int/Poor	23/61/17	32 / 55 / 13	22 / 58/ 20	31 / 59 / 9
Sarc features	13	18	12	8
PD-L1 positive			25.5	
Prior CN	82	83	69	74
ORR	42	59	56 (vs 27)	71
CR	9	6	8 (vs 4.6)	16
Median PFS	11.2 (vs 8.3)	15.4 (vs 11.1)	16.6 (vs 8.3)	23.9 (vs 9.2)
HR	0.7 (0.65-0.90) (int/poor)	0.69 (0.6-0.8)	0.51 (0.41-0.64)	0.39 (0.3-0.5)
1 yr OS			86% vs 76%	
Median OS	48.1	NR	NR	NR
Sunitinib arm	28.6	35.7	NR	NR
HR	0.66 (0.5-0.8) (int/poor)	0.53 (0.4-0.7)	0.60 (0.4-0.9)	0.66 (0.5-0.9)
PRO's	Pos	Neg	Pos	?
>= Gr 3 TRAE	48 vs 64	63 vs 58	61 vs 51	72 vs 59
>=3 transaminitis			10%	
>=3 MTN			12.5%	
Steroids			19%	



c/o Dr. Tracy Rose, UNC

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SWOG 1500

Sunitinib versus cabozantinib, crizotinib or savolitinib in metastatic papillary renal cell carcinoma (pRCC): Results from the randomized phase II SWOG 1500 study

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SWOG 1500

Key Eligibility

- Pathologically verified PRCC
- Available tissue submission for retrospective central adjudication of PRCC subtype
- Up to one prior systemic therapy, excluding VEGF- or MET-directed agents
- Zubrod performance status of 0-1
- Adequate organ and marrow function

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SWOG 1500

Results: Accrual and Futility Analysis

- From April 2016 to December 2019, 152 patients were enrolled at 65 centers throughout the US and Canada

mPRCC

- Histologically confirmed diagnosis of PRCC
- Measurable disease
- 0-1 prior lines of therapy
- No prior therapy with sunitinib
- Zubrod 0-1

Sunitinib

Cabozantinib

Crizotinib

Savolitinib

Primary Endpoint:

- Progression-free survival

Secondary Endpoints:

- Overall survival
- Response rate
- Adverse events
- Exploratory evaluation of:
 - MET mutational status
 - MET expression

• Savolitinib and crizotinib arms closed for futility in December of 2019

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SWOG 1500

Results: Progression-Free Survival

Progression-Free Survival
(See text for details)

Arm	n	Median PFS (mo)	95% CI	P-value
Cabozantinib	75	10.1	8.1-12.1	0.0001
Sunitinib	75	6.1	4.1-8.1	0.0001
Crizotinib	25	4.1	2.1-6.1	0.0001
Savolitinib	25	3.1	1.1-5.1	0.0001

• Cabozantinib significantly prolonged PFS relative to sunitinib (HR 0.60 [95%CI 0.37-0.97] [1-sided P-value=0.019])

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SWOG 1500

Results: Efficacy

	Sunitinib [n (%)]	Cabozantinib [n (%)]	Crizotinib [n (%)]	Savolitinib [n (%)]
Complete Response	0 (0)	2 (5)	0 (0)	0 (0)
Partial Response (PR)	2 (4)	8 (18)	0 (0)	1 (3)
Unconfirmed Partial Response	1 (2)	2 (5)	1 (4)	2 (7)
Stable Disease	23 (50)	23 (51)	7 (25)	8 (26)
Increasing Disease	11 (24)	4 (9)	12 (43)	8 (26)
Symptomatic Deterioration	1 (2)	1 (2)	3 (11)	1 (3)
Early Death	1 (2)	1 (2)	0 (0)	0 (0)
Assessment Inadequate	7 (15)	3 (7)	5 (18)	9 (31)
Total	46 (100)	44 (100)	28 (100)	29 (100)

Confirmed overall response rate with cabozantinib (23%) significantly higher than with sunitinib (4%) (2-sided P-value= 0.010)

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SWOG 1500 – Practice changing as new standard for pRCC

Conclusions

- SWOG 1500 is the first randomized trial exclusively in patients with metastatic pRCC to complete accrual
- Cabozantinib was shown to significantly prolong PFS relative to sunitinib, meeting the study's primary endpoint (HR 0.60 (95%CI 0.37-0.97 [1-sided P-value=0.019])
- Cabozantinib also significantly increased response rate relative to sunitinib (23% vs. 4% [2-sided P-value=0.010])
- Savolitinib and crizotinib study arms were terminated prematurely in a futility analysis; neither showed benefit in PFS relative to sunitinib
- Regardless of subtype classification (by either local or central review), cabozantinib had a homogeneous treatment effect across subtypes
- Cabozantinib should be considered the new reference standard for systemic therapy in patients with metastatic pRCC

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2021 GU Cancers Symposium Highlights

• Thank you for your attention.



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