The State of Cancer Care: Reflections from the 2017 ASCO Annual Meeting

Margaret Tempero, M.D.
Director, Pancreas Center, University of California, San Francisco
Editor-in-Chief, Journal of the National Comprehensive Cancer Network
&
Wes Kidder, M.D. , M.P.H.
Clinical Fellow, University of California, San Francisco

Overview

- Opening remarks by Dr. Margaret Tempero
- Highlights from the 2017 ASCO Annual Meeting
  - Selected Plenary Sessions
    - OlympiAD Study – *Dr. Mark Robson*
    - LATITUDE Study – *Dr. Karim Fazazi*
    - Patient reported outcomes for symptom monitoring – *Dr. Ethan Basch*
  - Selected Late Breaking Abstracts
    - STREAM Study – *Dr. Viviane Hess*
    - CALM Study – *Dr. Gary Rodin*
    - BCMA CAR-T cells in patients with relapse refractory MM – *Dr. Wanhong Zhao*
- Conclusions and Final Thoughts
- Questions/Comments

OlympiAD: Phase III trial of olaparib monotherapy versus chemotherapy for patients with HER2-negative metastatic breast cancer and a germline *BRCA* mutation

Mark Robson,[1] Seock-Ah Im,[2] Elżbieta Senkus,[3] Binghe Xu,[4] Susan M Domchek,[5] Norikazu Masuda,[6] Suzette Delaloge,[7] Wei Li,[8] Nadine Tung,[9] Anne Armstrong,[10] Wenting Wu,[11] Carsten Goessl,[11] Sarah Runswick,[12] Pierfranco Conte[13]

[1]Memorial Sloan Kettering Cancer Center, New York, USA; [2]Seoul National University Hospital, Seoul, Korea; [3]Medical University of Gdańsk, Gdańsk, Poland; [4]Cancer Hospital, Chinese Academy of Medical Sciences, Beijing, China; [5]Basser Center, University of Pennsylvania, Philadelphia, USA; [6]National Hospital Organization, Osaka National Hospital, Osaka, Japan; [7]Institut Gustave Roussy, Villejuif, France; [8]The First Hospital of Jilin University, Changchun, China; [9]Beth Israel Deaconess Medical Center, Dana-Farber Harvard Cancer Center, Boston, USA; [10]Christie Hospital NHS Foundation Trust, Manchester, UK; [11]AstraZeneca, Gaithersburg, USA; [12]AstraZeneca, Macclesfield, UK; [13]University of Padova and Istituto Oncologico Veneto IRCCS, Padova, Italy

ClinicalTrials.gov identifier: NCT02000622. This study was sponsored by AstraZeneca

Presented By Mark Robson at 2017 ASCO Annual Meeting

Phase II studies of olaparib in breast cancer

	Tutt *et al*[1] (n=54)	Gelmon *et al*[2] (n=26, 10 g*BRCA*m)	Kaufman *et al*[3] (n=62)
Patient population	Locally advanced/ metastatic *BRCA*m BC, ≥1 chemotherapy regimen	Advanced metastatic or recurrent BC, triple negative or known *BRCA*m	Advanced *BRCA*m BC that progressed despite ≥3 previous lines of chemotherapy for advanced/metastatic BC
Prior lines of therapy for advanced disease	3 (median, including adjuvant)	3 (median, including adjuvant)	4.6 (mean, metastatic only)
ORR	41%	0% (50% unconfirmed in *BRCA*m)	13%
Median DoR	144 days	–	204 days

BC, breast cancer; DoR, duration of response; ORR, objective response rate

1. Tutt A *et al Lancet* 2010;376:235–244; 2. Gelmon KA *et al Lancet Oncol* 2011;12:852–861; 3. Kaufman B *et al J Clin Oncol* 2015;33:244–250

Presented By Mark Robson at 2017 ASCO Annual Meeting

OlympiAD study design

- HER2-negative metastatic BC
  - ER+ and/or PR+ or TNBC
- Deleterious or suspected deleterious g*BRCA*m
- Prior anthracycline and taxane
- ≤2 prior chemotherapy lines in metastatic setting
- HR+ disease progressed on ≥1 endocrine therapy, or not suitable
- If prior platinum use
  - No evidence of progression during treatment in the advanced setting
  - ≥12 months since (neo)adjuvant treatment

Olaparib
300 mg tablets bd

2:1 randomization

Chemotherapy treatment of physician's choice (TPC)
- Capecitabine
- Eribulin
- Vinorelbine

Treat until progression

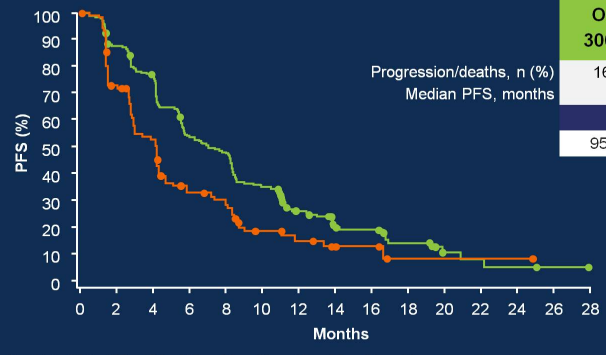
Primary endpoint:
- Progression-free survival (RECIST 1.1, BICR)

Secondary endpoints:
- Time to second progression or death
- Overall survival
- Objective response rate
- Safety and tolerability
- Global HRQoL (EORTC-QLQ-C30)

BICR, blinded independent central review; ER, estrogen receptor; HRQoL, health-related quality of life; PR, progesterone receptor; RECIST, response evaluation criteria in solid tumors; TNBC, triple negative breast cancer

Presented By Mark Robson at 2017 ASCO Annual Meeting

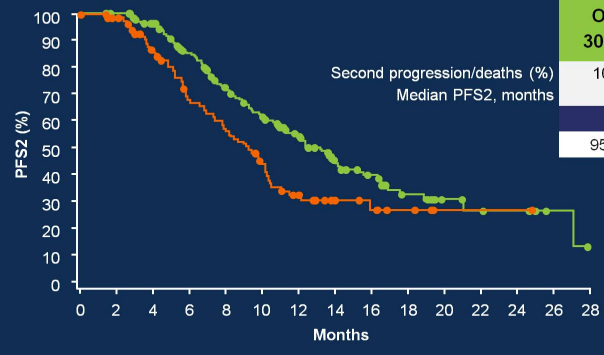
Primary endpoint: progression-free survival by BICR



	Olaparib 300 mg bd	Chemotherapy TPC
Progression/deaths, n (%)	163 (79.5)	71 (73.2)
Median PFS, months	7.0	4.2
HR 0.58		
95% CI 0.43 to 0.80; *P*=0.0009		

Presented By Mark Robson at 2017 ASCO Annual Meeting

Time to second progression or death (PFS2) by investigator assessment

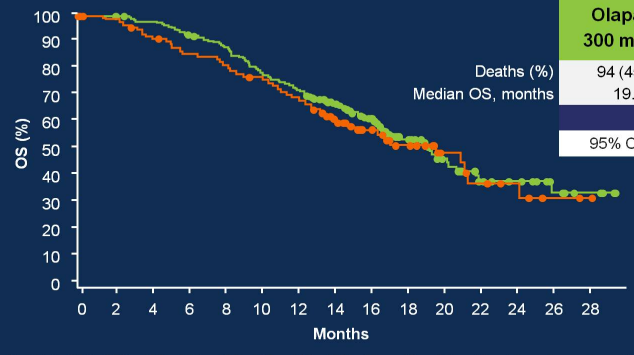


	Olaparib 300 mg bd	Chemotherapy TPC
Second progression/deaths (%)	104 (50.7)	53 (54.6)
Median PFS2, months	13.2	9.3
HR 0.57		
95% CI 0.40 to 0.83; *P*=0.0033		

At risk, n															
Olaparib 300 mg bd	205	199	185	152	123	102	75	44	34	18	8	6	5	2	0
Chemotherapy TPC	97	85	69	51	42	31	19	10	7	4	1	1	1	0	0

Presented By Mark Robson at 2017 ASCO Annual Meeting

Overall survival (interim analysis; 46% data maturity)

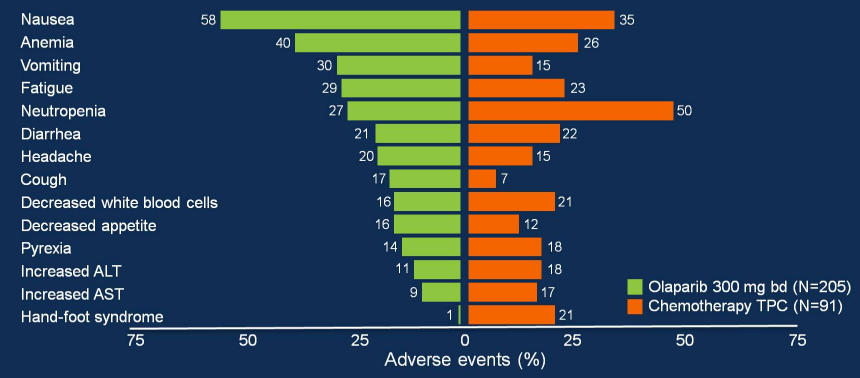


	Olaparib 300 mg bd	Chemotherapy TPC
Deaths (%)	94 (45.9)	46 (47.4)
Median OS, months	19.3	19.6
HR 0.90		
95% CI 0.63 to 1.29; *P*=0.5665		

At risk, n															
Olaparib 300 mg bd	205	205	199	189	178	159	146	109	78	46	30	18	14	8	4	0
Chemotherapy TPC	97	92	85	78	74	69	62	50	34	24	13	9	7	4	2	0

Presented By Mark Robson at 2017 ASCO Annual Meeting

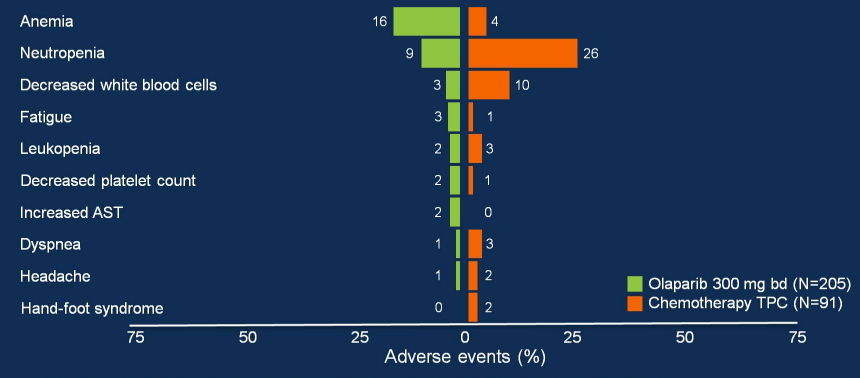
Adverse events (any grade) in ≥15% of patients



Irrespective of causality. MedDRA preferred terms for adverse events have been combined for 1) anemia and 2) neutropenia
ALT, alanine aminotransferase; AST, aspartate aminotransferase

Presented By Mark Robson at 2017 ASCO Annual Meeting

Grade ≥3 adverse events in ≥2% patients in either arm



Irrespective of causality. MedDRA preferred terms for adverse events have been combined for 1) anemia and 2) neutropenia
ALT, alanine aminotransferase; AST, aspartate aminotransferase

Presented By Mark Robson at 2017 ASCO Annual Meeting

Conclusions

- Olaparib tablet monotherapy provided a statistically significant and clinically meaningful PFS benefit versus standard-of-care chemotherapy for patients with HER2-negative metastatic breast cancer and a g*BRCA*m
- Olaparib was generally well tolerated with <5% discontinuing treatment for toxicity and a lower rate of Grade ≥3 AEs compared with chemotherapy
- OlympiAD is the first Phase III study in metastatic breast cancer patients demonstrating benefit for a PARP inhibitor over an active comparator

Presented By Mark Robson at 2017 ASCO Annual Meeting

LATITUDE: A phase 3, double-blind, randomized trial of androgen deprivation therapy with abiraterone acetate plus prednisone or placebos in newly diagnosed high-risk metastatic hormone-naïve prostate cancer patients

Karim Fizazi,[1] NamPhuong Tran,[2] Luis Fein,[3] Nobuaki Matsubara,[4] Alfredo Rodriguez-Antolin,[5] Boris Y. Alekseev,[6] Mustafa Özgüroğlu,[7] Dingwei Ye,[8] Susan Feyerabend,[9] Andrew Protheroe,[10] Peter De Porre,[11] Thian Kheoh,[12] Youn C. Park,[13] Mary B. Todd,[14] Kim N. Chi,[15] on behalf of the LATITUDE Investigators

[1]Gustave Roussy, University of Paris Sud, Villejuif, France; [2]Janssen Research & Development, Los Angeles, CA; [3]Instituto de Oncologia de Rosário, Rosário, Argentina; [4]National Cancer Center Hospital East, Chiba, Japan; [5]12 de Octubre University Hospital, Madrid, Spain; [6]P. A. Hertsen Moscow Cancer Research Institute, Moscow, Russian Federation; [7]Cerrahpaşa Medical Faculty, Istanbul University, Istanbul, Turkey; [8]Fudan University Shanghai Cancer Center, China; [9]Studienpraxis Urologie, Nürtingen, Germany; [10]Oxford University Hospitals Foundation NHS Trust, Oxford, UK; [11]Janssen Research & Development, Beerse, Belgium; [12]Janssen Research & Development, San Diego, CA; [13]Janssen Research & Development, Raritan, NJ; [14]Janssen Global Services, Raritan, NJ; [15]BC Cancer Agency, Vancouver, BC, Canada

Presented By Karim Fizazi at 2017 ASCO Annual Meeting

ADT + docetaxel: a new standard of care for men with mCNPC and high metastatic burden (2015)

Overall Survival	ADT + DOC	ADT		
	Median (mos)	Median (mos)	HR (95% CI)	*P* Value
GETUG-15[1]	62.1	48.6	0.88 (0.68-1.14)	0.3
CHAARTED[2]	57.6	47.2	0.73 (0.59-0.89)	0.0018
STAMPEDE[3]	60	45	0.76 (0.62-0.92)	0.005

1. Gravis G, et al. *Eur Urol*. 2016;70:256-262. 2. Sweeney C, et al. *N Engl J Med*. 2015;373:737-746; Sweeney C, et al. *Ann Oncol*. 2018;27(Suppl 6):243-265. 3. James N, et al. *Lancet*. 2016;387:1163-1177 and Vale C, et al. *Lancet Oncol* 2016;17:243-256.

Presented By Karim Fizazi at 2017 ASCO Annual Meeting

Objective

To evaluate the addition of AA + P to ADT on clinical benefit in men with newly diagnosed, high-risk, mCNPC

High-risk defined as meeting at least 2 of 3 high-risk criteria:
- Gleason score of ≥ 8
- Presence of ≥ 3 lesions on bone scan
- Presence of measurable visceral lesion

Presented By Karim Fizazi at 2017 ASCO Annual Meeting

Overall study design of LATITUDE

Patients
- Newly diagnosed adult men with high-risk mHNPC

Stratification factors
- Presence of visceral disease (yes/no)
- ECOG PS (0, 1 vs 2)

RANDOMIZED 1:1

- ADT + Abiraterone acetate 1000 mg QD + Prednisone 5 mg QD (n = 597)
- ADT + placebos (n = 602)

Efficacy end points

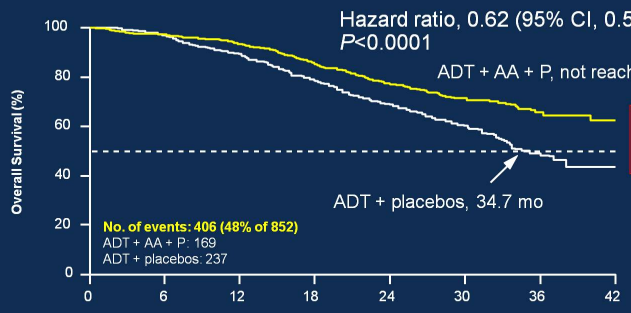
Co-primary:
- OS
- rPFS

Secondary: time to
- pain progression
- PSA progression
- next symptomatic skeletal event
- chemotherapy
- subsequent PC therapy

- Conducted at 235 sites in 34 countries in Europe, Asia-Pacific, Latin America, and Canada
- Designed and fully enrolled prior to publication of CHAARTED/STAMPEDE results

Presented By Karim Fizazi at 2017 ASCO Annual Meeting

Statistically significant 38% risk reduction of death



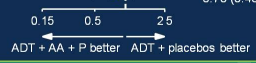
OS rate at 3 years:
ADT + AA + P: 66%
ADT + placebos: 49%

Median follow-up: 30.4 months

Presented By Karim Fizazi at 2017 ASCO Annual Meeting

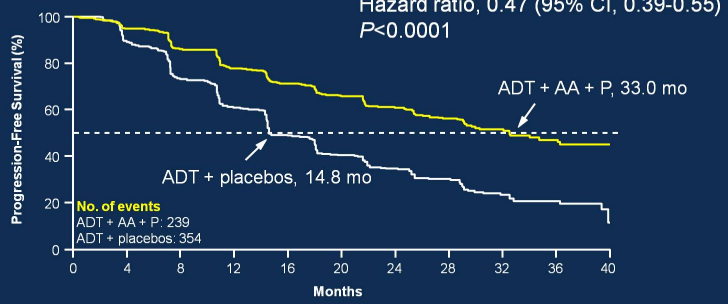
OS benefit consistently favorable across subgroups

Subgroup	ADT + AA + P	ADT + placebos	Hazard ratio (95% CI)
	Median (mo)		
All patients	NR	34.7	0.63 (0.51-0.76)
ECOG			
0	NR	38.2	0.64 (0.48-0.86)
1-2	NR	31.3	0.61 (0.46-0.79)
Visceral disease			
Yes	NR	32.3	0.51 (0.33-0.79)
No	NR	35.1	0.66 (0.53-0.83)
Gleason score			
< 8	NR	NR	0.62 (0.18-2.11)
≥ 8	NR	34.7	0.63 (0.51-0.77)
Bone lesions			
≤ 10	NR	NR	0.65 (0.45-0.96)
> 10	NR	31.3	0.60 (0.47-0.75)
Region			
Asia	NR	NR	0.73 (0.42-1.27)
East Europe	NR	30.5	0.50 (0.36-0.69)
West Europe	NR	38.1	0.75 (0.51-1.09)
Rest of world	NR	31	0.70 (0.45-1.09)



Presented By Karim Fizazi at 2017 ASCO Annual Meeting

Statistically significant 53% risk reduction of radiographic progression or death



No. at risk											
ADT + AA + P	597	533	464	400	353	316	251	177	102	51	21
ADT + placebos	602	488	367	289	214	168	127	81	41	17	7

Presented By Karim Fizazi at 2017 ASCO Annual Meeting

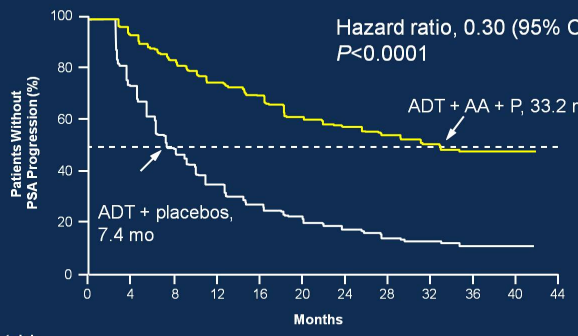
Statistically significant improvement in all secondary end points

Secondary End Points	ADT + AA + P (n = 597) Median (months)	ADT + placebos (n = 602) Median (months)	HR (95% CI)	*P* Value
Time to PSA progression	33.2	7.4	0.30 (0.26-0.35)	<0.0001
Time to pain progression	NR	16.6	0.70 (0.58-0.83)	<0.0001
Time to next symptomatic skeletal event	NR	NR	0.70 (0.54-0.92)	0.0086
Time to chemotherapy	NR	38.9	0.44 (0.35-0.56)	<0.0001
Time to subsequent prostate cancer therapy	NR	21.6	0.42 (0.35-0.50)	<0.0001

NR = not reached.

Presented By Karim Fizazi at 2017 ASCO Annual Meeting

Statistically significant 70% risk reduction of time to PSA progression

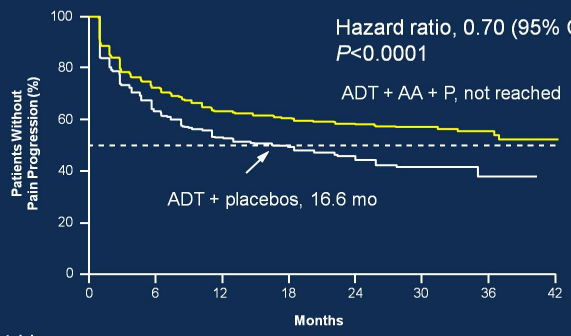


No. at risk

ADT + AA + P	597	520	447	379	340	285	227	162	95	48	18	0
ADT + placebos	602	393	250	172	129	102	65	33	19	8	5	0

Presented By Karim Fizazi at 2017 ASCO Annual Meeting

Statistically significant 30% risk reduction of time to pain progression

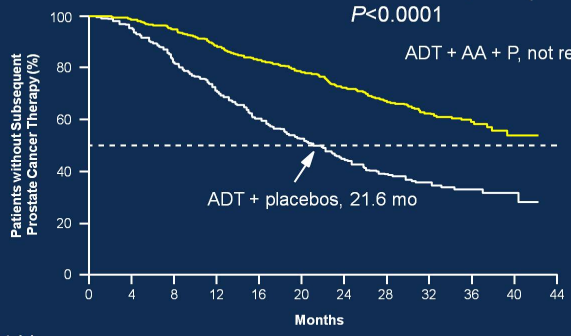


No. at risk

ADT + AA + P	597	395	297	247	181	96	39	2
ADT + placebos	602	332	211	137	82	36	7	0

Presented By Karim Fizazi at 2017 ASCO Annual Meeting

Statistically significant 58% risk reduction of time to subsequent PC therapy



No. at risk

ADT + AA + P	597	569	531	483	442	399	327	236	141	72	25	0
ADT + placebos	602	558	452	379	299	239	180	116	67	27	10	0

Presented By Karim Fizazi at 2017 ASCO Annual Meeting

Adverse events of special interest

Adverse Events	ADT + AA + P (n = 597)		ADT + placebos (n = 602)	
	Grade 3	Grade 4	Grade 3	Grade 4
	%		%	
Hypertension	20	0	10	0.2
Hypokalemia	10	0.8	1	0.2
ALT increased	5	0.3	1	0
AST increased	4	0.2	1	0
Hyperglycemia	4	0.2	3	0
Bone pain	3	0	3	0
Cardiac disorder	3	0.8	1	0
Anemia	2	0.5	4	0.2
Back pain	2	0	3	0
Fatigue	2	0	2	0
Spinal cord compression	2	0	1	0.5

Presented By Karim Fizazi at 2017 ASCO Annual Meeting

Conclusions

- In the phase 3 LATITUDE, addition of AA + P to ADT led to:
  - Significantly improved OS with a 38% reduction in the risk of death
  - Significantly prolonged rPFS (53% reduction) and all secondary end points
- The overall safety profile of ADT + AA + P was consistent with prior studies in patients with mCRPC

Presented By Karim Fizazi at 2017 ASCO Annual Meeting

Overall survival results of a randomized trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment (NCT00578006)

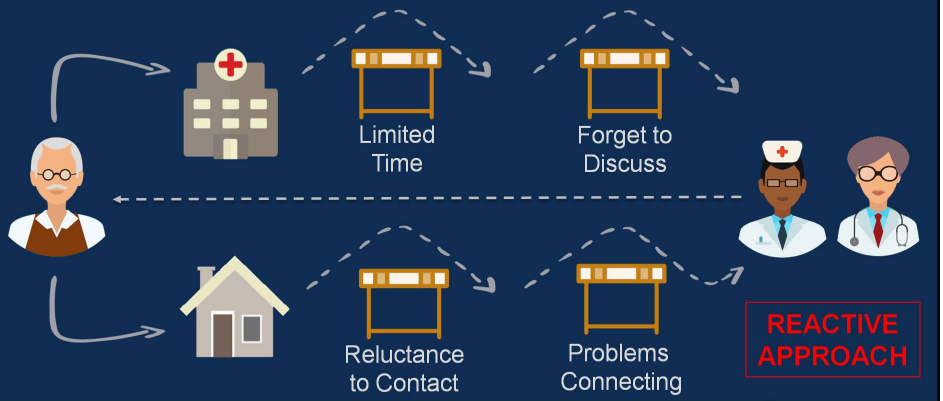
Ethan Basch, Allison Deal, Amylou Dueck, Antonia Bennett, Thomas Atkinson, Howard Scher, Mark Kris, Clifford Hudis, Paul Sabbatini, Dorothy Dulko, Lauren Rogak, Allison Barz, Deborah Schrag

From: Lineberger Comprehensive Cancer Center, University of North Carolina; Memorial Sloan Kettering Cancer Center; Mayo Clinic; Dana-Farber Cancer Institute

PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17

Presented By Ethan Basch at 2017 ASCO Annual Meeting

Standard Approach to Symptom Monitoring



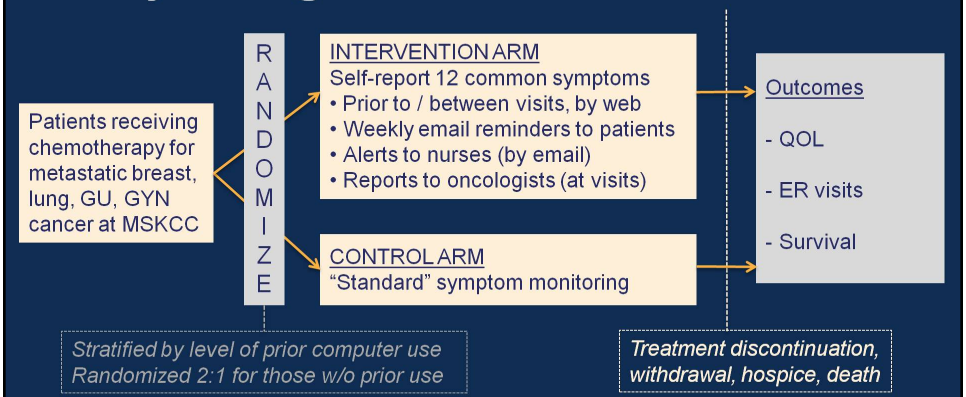
PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17 Presented by: Ethan Basch, MD

Presented By Ethan Basch at 2017 ASCO Annual Meeting

Alternative: Systematic Symptom Monitoring

Presented By Ethan Basch at 2017 ASCO Annual Meeting

Study Design



Presented By Ethan Basch at 2017 ASCO Annual Meeting

Patient Self-Reporting Interface

- Example: Pain

None	I have not had pain.
Grade 1 (Mild)	I have had mild pain, but it does not interfere with my normal functioning.
Grade 2 (Moderate)	I have had moderate pain, and my pain or my use of pain medications interferes with my normal functioning. But I am still able to carry out my normal daily activities.
Grade 3 (Severe)	I have had severe pain, and my pain or my use of pain medications severely interferes with my normal daily activities.
Grade 4 (Disabling)	My pain has been disabling.

Presented By Ethan Basch at 2017 ASCO Annual Meeting

Statistics

- Primary outcome: QOL, measured by EQ-5D
  - 80% power to detect an effect size of 0.40 for change from baseline to 6 months between arms (t-test, two-sided alpha 0.05)
  - *Analysis previously reported (J Clin Oncol 2016;34:557-565)*
- Overall survival
  - Ascertained from National Death Index
  - Estimated using Kaplan-Meier method
  - Compared between arms using a log-rank test and Cox proportional hazards regression adjusting for age, sex, race, education level, level of prior computer/email experience, cancer type

Presented By Ethan Basch at 2017 ASCO Annual Meeting

Patient Participation

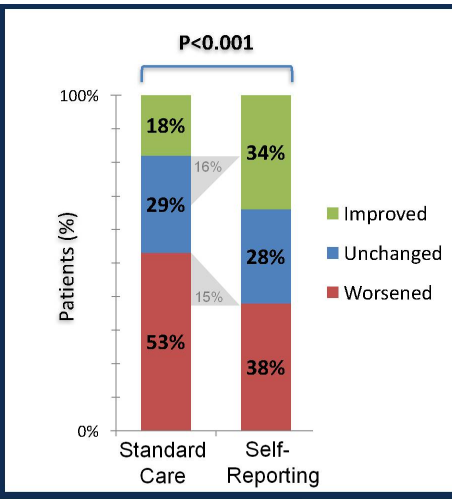
- Patients self-reported symptoms 73% of the time when prompted to do so
- Nurses took action in response to alerts 77% of the time
  - Counselling, supportive medications, referrals to ER, chemotherapy dose modifications, imaging

Presented By Ethan Basch at 2017 ASCO Annual Meeting

Quality of Life

- Assessed at 6 months, compared to baseline
- Compared to standard care, 31% more patients in the self-reporting arm experienced QOL benefits (*P<0.001*)

Basch: J Clin Oncol 2016;34:557-565



Presented By Ethan Basch at 2017 ASCO Annual Meeting

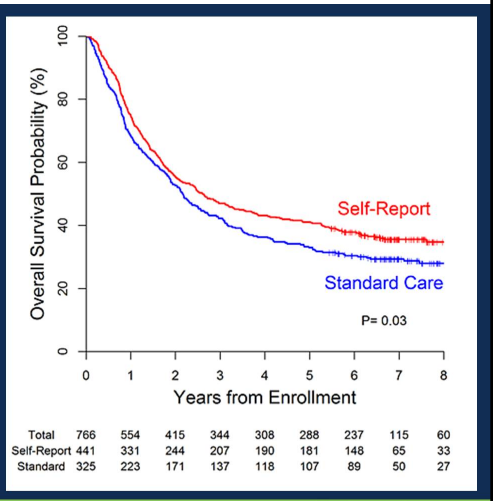
Proportion of Patients Visiting Emergency Room

- Compared to standard care, 7% fewer patients in the self-reporting arm visited the ER, with durable effects throughout the study (*P=0.02*)

Presented By Ethan Basch at 2017 ASCO Annual Meeting

Overall Survival

- Compared to standard care, median survival was 5 months longer among patients in the self-reporting arm (31.2 vs. 26.0 months) (*P=0.03*)
- Remained significant in multivariable analysis: Adjusted hazard ratio 0.832 (*95% CI; 0.696, 0.995*)

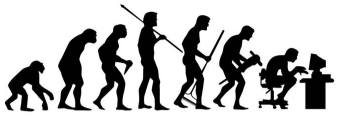


Presented By Ethan Basch at 2017 ASCO Annual Meeting

Conclusions

- Systematic symptom monitoring with patient self-reporting improves overall survival
- This approach should be considered for inclusion as a part of standard symptom management
- Future efforts should focus on implementation strategies for integrating self-reporting into electronic health records and into workflow of oncology practice

Presented By Ethan Basch at 2017 ASCO Annual Meeting



Web-based stress management for newly diagnosed cancer patients (STREAM): A randomized, wait-list controlled intervention study.

ClinicalTrials.gov NCT02289014

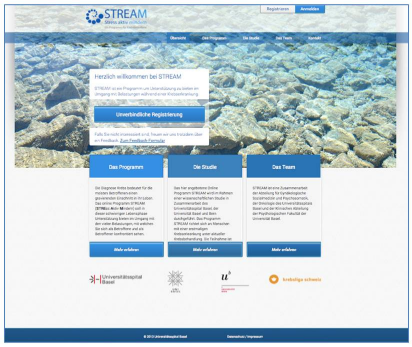
Viviane Hess MD
Medical Oncology
University Hospital Basel, Switzerland

Presented By Viviane Hess at 2017 ASCO Annual Meeting

STREAM Intervention

www.stress-aktiv-mindern.ch

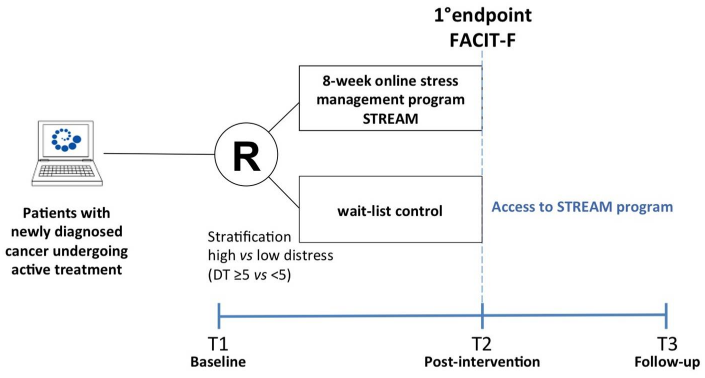
- 8-week program (8 modules)
  1-2 hours per week
- Based on established stress management programs[1]
- Therapist-guided: once weekly written contact with psychologist



[1]Antoni MH. Stress Management Intervention for Women with Breast Cancer. Baltimore: United Book Press; 2003.

Presented By Viviane Hess at 2017 ASCO Annual Meeting

Study design



Presented By Viviane Hess at 2017 ASCO Annual Meeting

Endpoints and Statistics

Efficacy endpoints

Primary endpoint: Quality of life FACIT-F total score at T2

Secondary endpoints: Distress (Distress Thermometer) and mood (HADS score) at T2

Efficacy analyses:

Analyses of Covariance (ANCOVAs)* in intention-to-treat population, significance level two-sided α 0.05

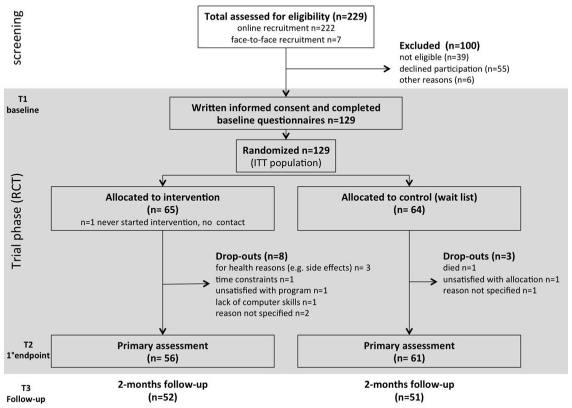
Sample Size

60 participants/arm, Δ 9 points FACIT-F score at T2, power 0.80, two-sided α 0.05

*ANCOVA with post-scores T2 as dependent variable, pre-scores T1 as covariate, group allocation (intervention vs control) as independent variable, adjusted for baseline distress (DT ≥ 5 vs <5)

Presented By Viviane Hess at 2017 ASCO Annual Meeting

Results
Patient flow



Presented By Viviane Hess at 2017 ASCO Annual Meeting

Results
Baseline characteristics

	All (n=129)	Control group (n=64)	Intervention group (n=65)
Age (median), years (IQR)	52 (46-58)	53 (46-58)	51 (46-57)
Sex	n (%)	n (%)	n (%)
female	109 (84.5%)	56 (87.5%)	53 (81.5%)
male	20 (15.5%)	8 (12.5%)	12 (18.5%)
Tumor origin			
breast	92 (71.3%)	47 (73.4%)	45 (69.2%)
gynecological tract	7 (5.4%)	5 (7.8%)	2 (3.1%)
lung	5 (3.9%)	3 (4.7%)	2 (3.1%)
CNS/head and neck	4 (3.1%)	1 (1.6%)	3 (4.6%)
lymphoma	11 (8.5%)	4 (6.2%)	7 (10.8%)
skin/soft tissue	1 (.8%)	1 (1.6%)	0 (0.0%)
gastrointestinal tract	7 (5.4%)	2 (3.1%)	5 (7.7%)
urogenital tract	2 (2%)	1 (1.6%)	1 (1.5%)
Disease stage			
Localized disease	111 (86.0%)	55 (85.9%)	56 (86.2%)
Metastatic disease	18 (14.0%)	9 (14.1%)	9 (13.8%)

Presented By Viviane Hess at 2017 ASCO Annual Meeting

Results
Baseline characteristics

	All (n=129)	Control group (n=64)	Intervention group (n=65)
Use of complementary medicine (n=116)			
Yes	31 (26.7%)	17 (30.4%)	14 (23.3%)
no	51 (44.0%)	23 (41.1%)	28 (46.7%)
I don't know	34 (29.3%)	16 (28.6%)	18 (30.0%)
Currently seeing a therapist			
Yes	45 (34.9%)	27 (42.2%)	18 (27.7%)
no	84 (65.1%)	37 (57.8%)	47 (72.3%)
Current use of psychotropic drugs			
Yes	17 (13.2%)	11 (17.2%)	6 (9.2%)
No	111 (86.0%)	53 (82.8%)	58 (89.2%)
I don't know	1 (0.8%)	0 (0%)	1 (1.5%)
Baseline FACIT-F score (IQR)	106.0 (84.2-123.0)	108.3 (87.8-124.0)	101.0 (81.0-120.0)
Baseline Distress (DT)			
low	30 (23.3%)	14 (21.9%)	16 (24.6%)
high (≥5 DT)	99 (76.7%)	50 (78.1%)	49 (75.4%)
Baseline HADS score (IQR)	12 (7-17)	12 (7-16)	13 (7-18)

Presented By Viviane Hess at 2017 ASCO Annual Meeting

Results
Intervention

	Intervention group (n=65)
Median duration, weeks (IQR)	**11.7 weeks (9.1 to 18.6)**
Adherence	
6 out of 8 modules	**52 (80.0%)**
All 8 modules	**49 (75.4%)**
Usability	
SUS score, module 1, mean (IQR)	**87.5 (81.2 to 95.0)**
SUS score, module 8, mean (IQR)	**90.0 (82.5 to 95.0)**
Therapeutic alliance	
WAI-SR score, mean (IQR)	**3.77 (3.38 to 4.14)**

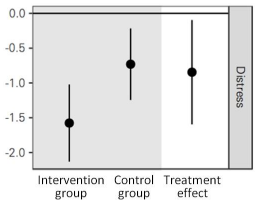
Therapists' time per patient / week minutes, mean (IQR)	**13.3 (IQR 9.5-17.9)**

Presented By Viviane Hess at 2017 ASCO Annual Meeting

Results
Efficacy outcomes*

*ANCOVAs T2-T1

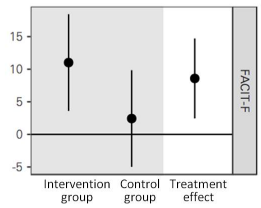
Distress



DT
Treatment effect, mean (95%CI)
-0.85
(-1.60;-0.10)
p = 0.03

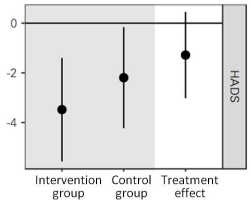
Quality of life

Primary endpoint



FACIT-F
Treatment effect, mean (95%CI)
8.59
(2.45 to 14.73)
p = 0.007

Mood



HADS
Treatment effect, mean (95%CI)
-1.28
(-3.02;0.45)
p = 0.15

Presented By Viviane Hess at 2017 ASCO Annual Meeting

Results
2-month Follow-up

Follow-up intervention group

FACIT-F, DT and HADS score did not change significantly between T2 and T3

Follow-up control group

51/64 patients underwent intervention after T2

	Mean change (95%CI)*	p-value
Quality of life (FACIT-F)	**10.95 (6.18 to15.71)**	<0.0001
Distress thermometer (DT)	**-1.25 (-1.95 to -0.55)**	0.001
Hospital Anxiety and Depression Scale (HADS)	**-2.83 (-4.29 to -1.36)**	0.0004

*paired t-test on ITT population (n=64) T2-T3

Presented By Viviane Hess at 2017 ASCO Annual Meeting

STREAM: Conclusions

- **Therapist-guided online stress management program for newly diagnosed cancer patients is feasible during treatment with a low drop out rate**
- **Cancer patients can be reached via online recruitment**
- **Majority of participants were female, breast cancer patients in the curative setting**
- **75% of patients had high levels of distress at baseline**
- **Therapist-guided online stress management program STREAM significantly improved quality of life including fatigue and lowered distress**

Presented By Viviane Hess at 2017 ASCO Annual Meeting

Managing Cancer And Living Meaningfully (CALM):
A Randomized Controlled Trial of a Psychological Intervention for Patients with Advanced Cancer

Gary Rodin MD, FRCPC
Head, Department of Supportive Care
Princess Margaret Cancer Centre

Co-Principal Investigators:

Sarah Hales MD, PhD, FRCPC
Psychiatrist, Department of Supportive Care
Princess Margaret Cancer Centre

Chris Lo PhD
Research Psychologist, Department of Supportive Care
Princess Margaret Cancer Centre

Funding: Canadian Institutes of Health Research

Presented By Gary Rodin at 2017 ASCO Annual Meeting

Managing Cancer And Living Meaningfully (CALM)

- A novel, brief supportive-expressive psychotherapy intervention
  - 3-6 individual sessions over 3-6 months with a specially trained cancer clinician
  - Relational support and reflective space
- Attention to four broad domains:
  - Symptom management & communication with healthcare providers
  - Changes in self and relationships with close others
  - Spirituality and sense of meaning and purpose
  - Future-oriented concerns, hope and mortality

Presented By Gary Rodin at 2017 ASCO Annual Meeting

Rationale for CALM

- Predictable and often overwhelming challenges
- Motivation for help heightened due to the perceived shortness of time
- Systematic and routine psychological interventions for patients with advanced disease are not implemented in most cancer centers
- Evidence has not been available to demonstrate the effectiveness of such interventions

Presented By Gary Rodin at 2017 ASCO Annual Meeting

Methods

- Unblinded RCT with two trial conditions:
  - CALM plus Usual Care (UC) or UC
- Participants:
  - Patients with advanced cancer recruited from ambulatory oncology clinics at a comprehensive cancer center
- Inclusion criteria:
  - ≥18 years of age
  - Fluent in English
  - No cognitive impairment
  - Confirmed diagnosis of advanced or metastatic cancer

Presented By Gary Rodin at 2017 ASCO Annual Meeting

Outcomes

- **Primary outcome:**
  - Severity of depressive symptoms (*Patient Health Questionnaire-9) (PHQ-9)*
- **Secondary outcomes included:**
  - Quality of life *(Quality of Life at the End-of-Life Cancer Scale) (QUAL-EC)*
  - Emotional support from healthcare providers *(Clinical Evaluation Questionnaire) (CEQ)*
  - Death anxiety (*Death and Dying Distress Scale) (DADDS)*
  - Generalized anxiety (*Generalized Anxiety Disorder-7) (GAD-7)*
  - Spiritual well-being (*Functional Assessment of Chronic Illness Therapy - Spiritual Well-Being Scale) (FACIT-Sp)*

Presented By Gary Rodin at 2017 ASCO Annual Meeting

Primary Outcome

Primary Outcome PHQ-9	UC Mean (SD)	CALM Mean (SD)	Δ_{M1-M2} *	CI (lower, upper)	*p*-value	Cohen's d
Baseline	7.41 (4.75) (n=154)	7.45 (4.96) (n=151)	-	-	-	-
3 months	7.01 (4.82) (n=128)	5.97 (4.83) (n=119)	1.09	0.04, 2.13	0.04	0.23
6 months	6.66 (4.96) (n=119)	5.35 (3.99) (n=107)	1.33	0.27, 2.38	0.01	0.30

*Δ_{M1-M2} is the regression-estimated mean difference between groups controlled for baseline

Presented By Gary Rodin at 2017 ASCO Annual Meeting

Clinical Importance

- The proportion of depressed individuals with a clinically meaningful reduction* in depressive symptoms:
  - 52% CALM vs. 33% UC at 3 months
  - 64% CALM vs. 35% UC at 6 months
- CALM participants were also:
  - Less likely to develop depressive symptoms of at least subthreshold severity at 3 months:
    - 13% CALM vs. 30% UC

* Minimal clinically important difference (MCID) ≥ 5 point reduction on PHQ-9

Presented By Gary Rodin at 2017 ASCO Annual Meeting

Secondary Outcomes

- Secondary outcomes which favored CALM at 3 and 6 months included:
  - Greater end-of-life preparation
  - Greater opportunity to talk about future-oriented concerns and feel less frightened
  - Greater ability to express and manage feelings
- Additional outcomes favoring CALM at 6 months included:
  - Better ability to talk and feel understood about how cancer has affected their life
  - Better ability to explore ways of communicating with the healthcare team & family
  - Better ability to deal with changes in relationships as a result of cancer
  - Greater clarification of values and beliefs
- All effects were strengthened at 6 months

Presented By Gary Rodin at 2017 ASCO Annual Meeting

Conclusions

- CALM is an effective intervention that alleviates depressive symptoms in individuals with advanced or metastatic cancer and helps them to address the multiple and predictable challenges that they face
- A global network is now being established to train health professionals in the delivery of this intervention and to evaluate its effectiveness in diverse clinical and cultural settings

Presented By Gary Rodin at 2017 ASCO Annual Meeting

Durable remissions with BCMA specific chimeric antigen receptor (CAR)-modified T cells in patients with refractory/relapsed multiple myeloma

Wanhong Zhao (alternative presenter)

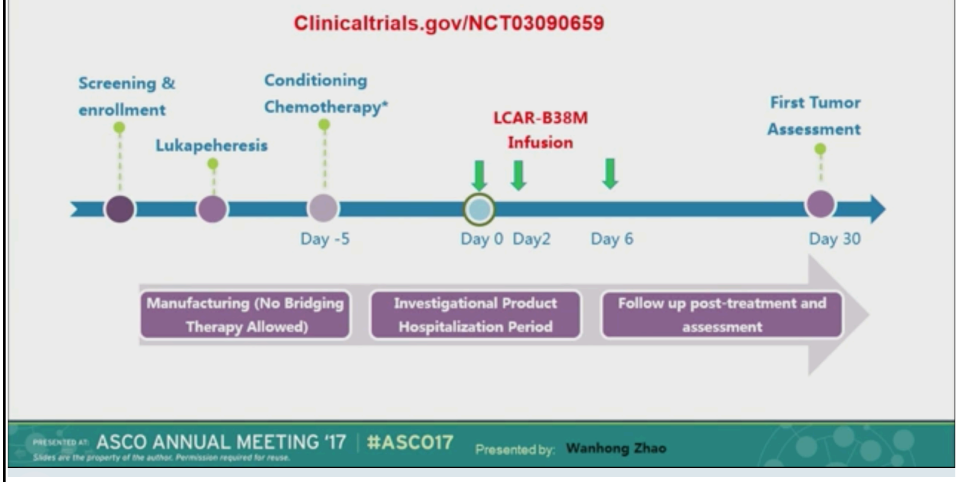
Frank (Xiaohu) Fan [1], Wanhong Zhao [2] Jie Liu [2], Aili He [2], Yinxia Chen [2], Xingmei Cao [2], Nan Yang [2], Baiyan Wang [2], Pengyu Zhang [2], Yilin Zhang [2], Fangxia Wang [2], Bo Lei [2], Liufang Gu [2], Xugeng Wang [2], Qiuchuan Zhuang [1] and Wanggang Zhang [2]

[1]Nanjing Legend Biotech Inc., Nanjing, China

[2]Hematology Division, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China

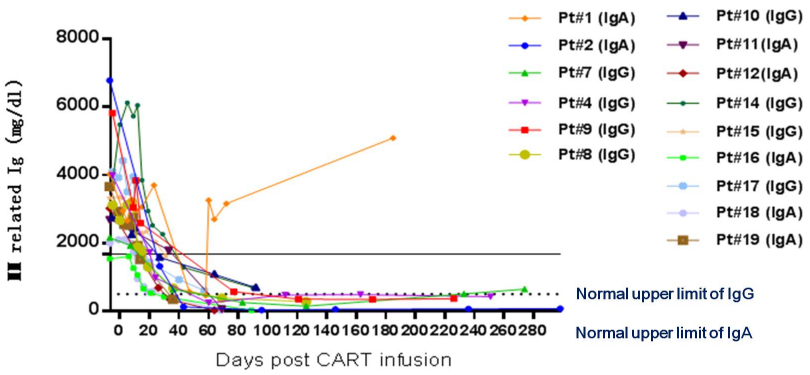
Presented By Wanhong Zhao at 2017 ASCO Annual Meeting

Legend LCAR-B38M Treatment Scheme



Presented By Wanhong Zhao at 2017 ASCO Annual Meeting

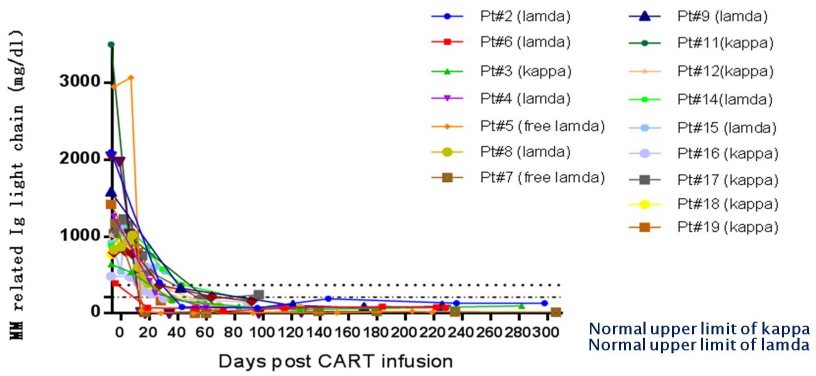
Clinical efficacy of LCAR-B38M product



PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17
Slides are the property of the author. Permission required for reuse.
Presented by: Wanhong Zhao

Presented By Wanhong Zhao at 2017 ASCO Annual Meeting

Clinical efficacy of LCAR-B38M product

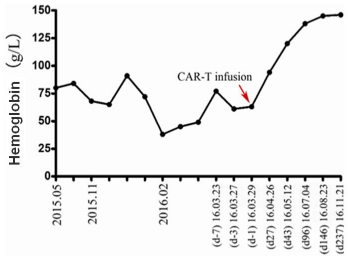


Presented By Wanhong Zhao at 2017 ASCO Annual Meeting

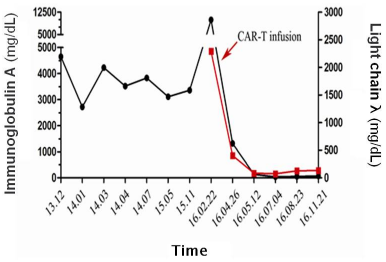
Legend's first CR case in MM CAR-T clinical trial

- Patient#2 follow-up (two months after CAR-T therapy)

Hb



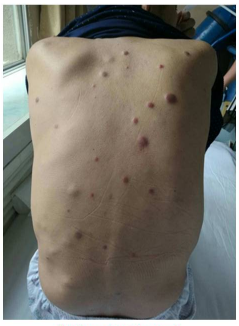
IgA (Lamda light chain)



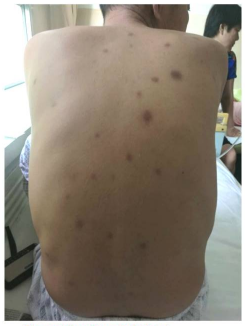
- ✓ All Hematology indexes recovered as normal;
- ✓ Tumor cells in bone marrow disappeared completely;
- ✓ Abnormal immunoglobulin disappeared.

Clinical efficacy of LCAR-B38M product

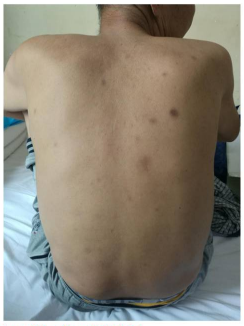
- The 6th MM patient had widely spread extramedullary lesion of metastases found all over the body before our treatment, but all lesions have disappeared after the treatment.



Before treatment



Day 18 after CAR-T

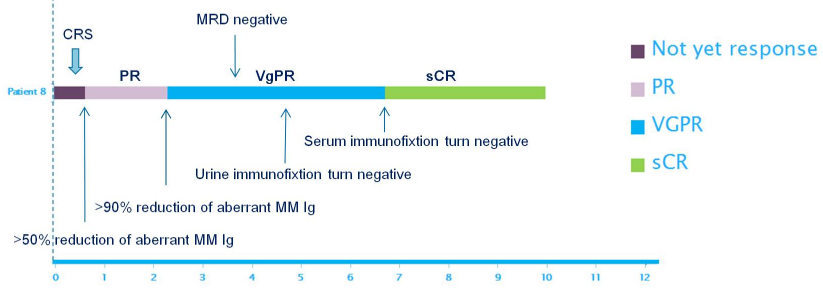


Day 83 after CAR-T

Presented By Wanhong Zhao at 2017 ASCO Annual Meeting

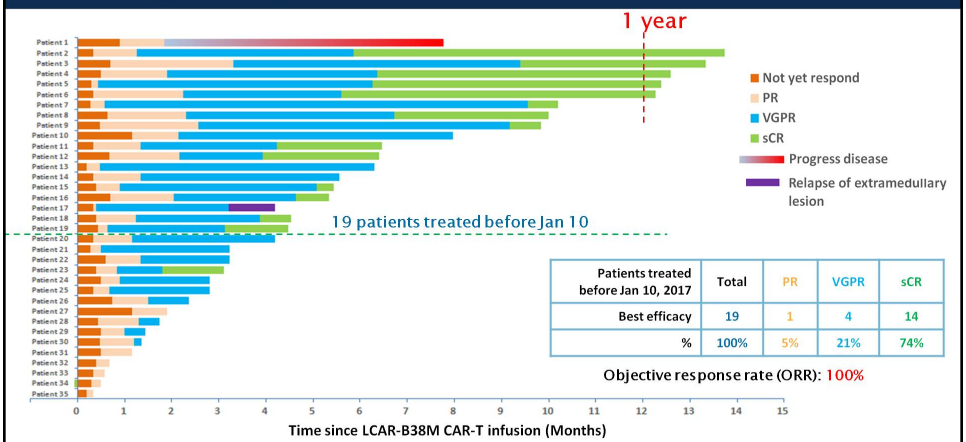
Efficacy follow-up of LCAR-B38M CAR-T cells

Typical outcome of treated patients in efficacy follow-up



Presented By Wanhong Zhao at 2017 ASCO Annual Meeting

Efficacy follow-up of LCAR-B38M CAR-T cells



Patients treated before Jan 10, 2017	Total	PR	VGPR	sCR
Best efficacy	19	1	4	14
%	100%	5%	21%	74%

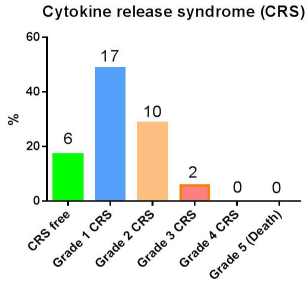
Objective response rate (ORR): 100%

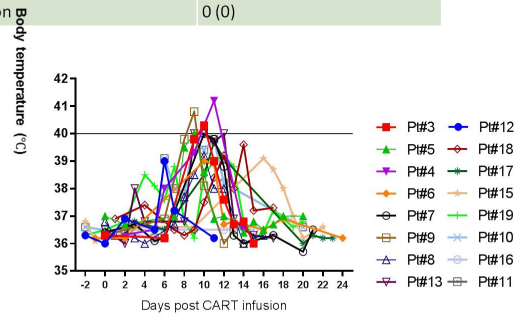
PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17 Presented by: Wanhong Zhao

Presented By Wanhong Zhao at 2017 ASCO Annual Meeting

Safety: Major adverse events is cytokine release syndrome (CRS)

Adverse Event, n (%)	Patients (N=35)
Grade ≥3 adverse event	2 (5.7%)
Serious adverse event	0 (0)
Fatal events excluding disease progression	0 (0)





PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17 Presented by: Wanhong Zhao

Presented By Wanhong Zhao at 2017 ASCO Annual Meeting

Conclusions

- LCAR-B38M CAR-T technology exert quick and reproducible therapeutic effects in refractory and relapsed multiple myeloma patients.
- >12 months follow-up of early patients shows durable and stringent complete remission which raises hopes of cure.
- LCAR-B38M technology not only demonstrate outstanding efficacy, but also suggest a great safety profile.
- US clinical trial is under way and the technology will be fully validated under "American (FDA) standard".

Presented By Wanhong Zhao at 2017 ASCO Annual Meeting

Questions?