Results. We reviewed 299 charts, with 198 (66.2%) included for analysis. The mean age was 70.4 ± 15.0 years, 53% female and 49.5% black. PCT testing was done in 72 (36%) patients; 117 (59%) had antimicrobials given in the emergency department (ED). If the PCT was performed, patients were more likely to receive antibiotics in the ED (79.2% vs. 47.6%, $P < 0.0001$). Patients who had a PCT drawn were less likely to have antibiotics continued after discharge from the ED (27.6% vs. 73.3%, $P < 0.0001$). The median duration of antimicrobials was shorter in patients who had a PCT level drawn than those who did not, 1 day (range 0.5–14) vs. 3 days (0.5–61), $P < 0.0001$. The duration of antimicrobials also tended to be shorter in patients with PCT levels ≤ 0.25 compared with those with levels >0.25, 0.5 days (0.5–12) vs. 1.0 day (0.5–14), p = 0.06.

Conclusion. Among patients with a discharge diagnosis of CHF, there was an association between the use of the PCT assay and both discontinuation of antibiotics given in the ED as well as decreased duration of antimicrobials in patients. These results support the ongoing use of this test to promote antimicrobial stewardship.

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2243. Using Host Biomarkers and Time to Blood Culture Positivity to Predict Necessity for Echocardiogram in Patients with *Staphylococcus aureus* Endocarditis

Graham Edwardson[1]; Cecilia Volk[1]; Victor Nizet, MD[2];
George Sakoulas, MD[3]; Warren Rose, PharmD, MPH[1]; [1]University of Wisconsin - Madison, Madison, Wisconsin; [2]University of California - San Diego, La Jolla, California; [3]University of California - San Diego, San Diego, California

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Background. Patients with complicated *S. aureus* bacteremia (SaB) require a transesophageal echocardiogram (TEE) to rule out endocarditis. Risks of TEE may exceed benefits in patients with a low pretest probability of endocarditis. Given our prior findings that endovascular bacterial burden drives elevated serum IL-10 concentrations, we hypothesize that time to positive blood culture and IL-10 serum concentrations may be used to risk stratify patients for selection of TEE. We compared time to positive blood culture and serum IL-10 in patients with negative and positive TEE.

Methods. Patients with SaB were included if they had a diagnosis of primary, endovascular infection source of bacteremia identified by an infectious diseases consult team and a TEE performed. A retrospective chart review was done to identify the time to positivity (hours) of patient blood cultures grown aerobically or anaerobically and TEE results. Sera collected at clinical presentation of these patients were tested for biomarkers IL-10 and IL-1β. Mann–Whitney U test compared the data between the two groups.

Results. This study included 66 patients with SaB: 17 with negative TEE and 49 with positive TEE. Patients with a positive TEE confirming endocarditis had a faster time to positive blood cultures compared with patients with negative TEE ($P = 0.031$; figure). IL-10 serum concentrations were significantly higher in patients with positive TEE (26.2 pg/mL) vs. negative TEE (14.39 pg/mL). Time-to-positivity in blood culture was linearly associated serum IL-10 concentrations ($P = 0.044$; figure). Serum IL-1β concentrations were also higher in TEE positive vs. TEE negative patients (32.1 vs. 14.7 pg/mL, $P = 0.067$).

Conclusion. These data lend further evidence to link high endovascular bacterial burden (measured by shorter time to positive blood culture) and serum IL-10 concentrations. As anticipated, patients with positive TEE had significantly shorter time to blood culture positivity and higher IL-10 serum concentrations than those with negative TEE. With further study on a larger number of patients, time to positive blood cultures and serum biomarkers like IL-10 may be used to risk stratify patients for performance of TEE, as well as to select antimicrobial therapy and to adjust treatment duration.

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2244. Clinical Outcomes with Extended Infusion (EI) vs. Intermittent Infusion (II) of Cefepime (FEP), Piperacillin/Tazobactam (TZP), and Meropenem (MEM) in Patients with Gram-Negative (GN) Bacteremia

Kieu-Nhi Tran, PharmD[1]; Ryan Mynatt, PharmD, BCPS-AQ ID[2];
Keith S. Kaye, MD, MPH[3]; Jason M. Pogue, PharmD, BCPS, BCIDP[4]; [1]Michigan Medicine, Detroit, Michigan; [2]Detroit Medical Center, Detroit, Michigan; [3]University of Michigan Medical School, Ann Arbor, Michigan; [4]University of Michigan College fo Pharmacy, Ann Arbor, Michigan

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Background. The increase in drug-resistant pathogens has prompted interest in dosing of β-lactams (BLs) via EI. Available data on this practice are conflicting, rarely assess non-critically ill patients or low MIC pathogens, and do not focus on outcomes other than clinical cure or mortality. Further assessment of this practice is warranted.

Methods. This is a retrospective cohort study of adult patients who received FEP, TZP, or MEM for GN bacteremia via INI or EI from 2010 to 2018. Patients were included if the pathogen was susceptible to the target BL and they received study drug within 24 hours of bacteremia onset and continued it for ≥ 48 hours. Patients were excluded if they had a mixed infection or received > 48 hours of combination therapy. Patients were matched 1:1 based on study drug utilized, sepsis severity, ICU status, bacteremia source, and causative pathogen. Outcomes assessed included time to clinical stabilization as well as treatment failure, mortality, length of stay (LOS), and recurrence.

Results. 268 patients (134 matched patients in each group) were included. Median (IQR) age of the cohort was 64 (55–77) years, and 57% were male. Common comorbidities were diabetes (35%) and CKD (26%), and the median (IQR) Charlson Comorbidity Index (CCI) was 3 (1–4). 40% of the population presented with severe sepsis or septic shock, and 42% were in the ICU at infection onset. Baseline characteristics were similar between the two groups except patients receiving EI were older (65.5 (58–78) vs. 61.5 (52–73); $P = 0.006$ and had higher median CCI (3 (2–4) vs. 2 (1–3); $P < 0.001$,) while patients in the II group had a higher mean weight (85.5 ± 27.8 vs. 78.8 ± 19.2, $P = 0.02$.) The most common organisms isolated were *E. coli* (41%), *K. pneumoniae* (18%), and *P. aeruginosa* (13%), and the most common source of infection was the urine (51%). Outcomes are listed in Table 1. EI was associated with decreases in time to defervescence, WBC normalization, and SIRS resolution. Furthermore, EI was associated with a lower incidence of treatment failure and recurrence as well as decreases in LOS and ICU-LOS. There was no difference in mortality.

Conclusion. The findings of this analysis highlight the role of EI in BL therapy as an important stewardship strategy to optimize clinical outcomes in all patients with GN bacteremia.

Table 1. Study outcomes

PRIMARY OUTCOME	Intermittent n = 134	Extended n = 134	P value
Time to defervescence, hours, median (IQR)	n = 45 30 (15.4-46.4)	n = 39 6.5 (2.3-15.9)	<0.001
Time to WBC normalization, hours, median (IQR)	n = 62 73.6 (41.5-176.0)	n = 52 39.3 (27.7-82.6)	0.003
Time to SIRS resolution, hours, median (IQR)	n = 92 52.8 (35.6-116.0)	n = 81 30 (10-43)	<0.001

SECONDARY OUTCOMES	Intermittent n = 134	Extended n = 134	P value
Hospital mortality, n (%)	0 (0)	4 (3.0)	0.122
Infection-related mortality, n (%)	0 (0)	1 (0.7)	1
Treatment failure, n (%)	13 (9.7)	1 (0.7)	0.001
LOS from antibiotic start, days, median (IQR)	9 (6-15)	6 (4-9)	<0.001
Duration of study antibiotic, days ± SD	5.1 ± 4.4	3.4 ± 2.0	<0.001
ICU LOS from antibiotic start, days, median (IQR)	n = 56 5 (3-9)	n = 56 3 (3-5)	<0.001
Recurrence of bloodstream infection, n (%)	9 (6.7)	0 (0)	0.003
Recurrence due to resistant isolate, n (%)	2 (1.5)	0 (0)	0.498

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2245. Oral 5-Day Lefamulin for Outpatient Management of Pneumonia Outcomes Research Team (PORT) Risk Class III/IV Community-Acquired Bacterial Pneumonia (CABP): Post Hoc Analysis of the Lefamulin Evaluation Against Pneumonia (LEAP) 2 Phase 3 Study

Jennifer Schranz, MD[1]; Elizabeth Alexander, MD, MSc, FIDSA[1];
David Fitts, MPH, PhD[1]; David Mariano, PharmD[1]; Andrew Meads, N/A[1];
Christian Sandrock, MD[2]; Gregory J. Moran, MD, FACEP[3];
Steven P. Gelone, PharmD[1]; [1]Nabriva Therapeutics US, Inc., King of Prussia, Pennsylvania; [2]UC Davis School of Medicine, Sacramento, California; [3]Olive View-UCLA Medical Center, Sylmar, California

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Background. Site-of-care decisions (e.g., admission vs. outpatient) in CABP management can be challenging for healthcare providers. Here we describe a post hoc analysis of adults with CABP managed as outpatients in the LEAP 2 double-blind, non-inferiority, Phase 3 trial.

Methods. LEAP 2 compared the efficacy and safety of oral lefamulin (LEF) 600 mg every 12 hours for 5 days vs. oral moxifloxacin (MOX) 400 mg every 24 hours for 7 days in adults with PORT Risk Class II-IV. Descriptive statistics were generated to characterize demographics, baseline characteristics, efficacy, and safety outcomes in the subpopulation of outpatients in LEAP 2.

Results. Overall, 42% (310/736) of patients started treatment as outpatients (41% [151/368] LEF and 43% [159/368] MOX). Age, gender, and BMI were generally similar in both treatment groups. 44% (66/151) LEF and 40% (64/159) MOX outpatients had PORT Risk Class III or IV, and 21% in both groups (31/151 LEF and 34/159 MOX) had CURB-65 score 2 or 3. Comorbidities included smoking history (43% LEF vs. 34% MOX), hypertension (26% vs. 30%), COPD/asthma (14% vs. 18%), and diabetes mellitus (7% vs. 11%). Early clinical response (ECR) responder rates and investigator's assessment of clinical response (IACR) success rates at the test of cure (TOC) visit were high and similar in both groups among all, PORT Risk Class III/IV, and CURB-65 score 2 or 3 outpatients (Table 1). In the PORT Risk Class III/IV subset, 86% LEF vs. 80% MOX patients were both an ECR responder and IACR success at TOC. In the CURB-65 score 2 or 3 subset, 87% LEF vs. 74% MOX patients were both an ECR responder and IACR success at TOC. Treatment-emergent adverse event (TEAE) rates were similar in both groups (Table 2). Consistent with overall study results, the difference between groups in related TEAEs was driven by gastrointestinal disorders (20% LEF vs. 5% MOX), specifically diarrhea (15% vs. 1%). Rates of TEAEs leading to discontinuation were low and similar in both groups. No LEF outpatient had an SAE or was admitted during the study, compared with 5 (3%) SAEs, including 2 deaths, in the MOX group.

Conclusion. These study data suggest that PORT Risk Class III or IV patients can be effectively managed as outpatients with 5 days of oral LEF as an alternative to fluoroquinolones for the treatment of CABP.

Table 1: Clinical Efficacy Outcomes (LEAP 2 Outpatients)

Subgroup Outcome	Lefamulin n/N (%)	Moxifloxacin n/N (%)
All Outpatients		
ECR Responder	138/151 (91.4)	142/159 (89.3)
IACR at TOC Success	138/151 (91.4)	143/159 (89.9)
PORT Risk Class III or IV Outpatients		
ECR Responder	59/66 (89.4)	56/64 (87.5)
IACR at TOC Success	60/66 (90.9)	58/64 (90.6)
CURB-65 Score 2 or 3 Outpatients		
ECR Responder	27/31 (87.1)	28/34 (82.4)
IACR at TOC Success	28/31 (90.3)	30/34 (88.2)

CURB-65=confusion, blood urea nitrogen>19 mg/dL (>6.8 mmol/L), respiratory rate
≥30 breaths/min, blood pressure <90 mmHg systolic or ≤60 mmHg diastolic, age ≥65 years;
ECR=early clinical response; IACR=investigator's assessment of clinical response;
PORT=pneumonia outcomes research team; TOC=test of cure

Table 2: Overall Summary of Adverse Events (LEAP 2 Outpatients)

Adverse Event	Lefamulin N=151 n (%)	Moxifloxacin N=159 n (%)
Treatment-emergent AE	52 (34.4)	48 (30.2)
Related TEAE	34 (22.5)	18 (11.3)
Serious TEAE	0	5 (3.1)
Related serious TEAE	0	0
TEAE leading to DC of study drug	4 (2.6)	4 (2.5)
Related TEAE leading to DC of study drug	2 (1.3)	1 (0.3)
TEAE leading to death	0	2 (1.3)

AE=adverse event; DC=discontinuation; TEAE=treatment-emergent adverse event

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2246. Improved Outcomes for Cancer Patients Treated With Ceftazidime–Avibactam vs. Polymyxin-Containing Regimens for Carbapenem-Resistant *Enterobacteriaceae* Bacteremia

Jovan Borjan, PharmD; Samuel A. Shelburne, MD, PhD;
Samuel A. Shelburne, MD, PhD; Micah M. Bhatti, MD, PhD;
Samuel L. Aitken, PharmD; Samuel L. Aitken, PharmD; The University of Texas MD Anderson Cancer Center, Houston, Texas

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Background. Outcomes are improved with ceftazidime–avibactam (CZA) compared with polymyxin-based regimens (PBR) for carbapenemase-producing carbapenem-resistant *Enterobacteriaceae*. It is unclear whether this finding is true in non-carbapenemase (non-CP) producing CRE. The purpose of this study was to compare the efficacy and safety of CZA-based and PBR for CRE bacteremia in cancer patients with a high prevalence of non-CP CRE.

Methods. Adult cancer patients with first occurrence of CRE (i.e., meropenem non-susceptible) bacteremia treated with either CZA or PBR as directed therapy were included. Day 14 integrated benefit-risk outcomes based on desirability of outcome ranking (DOOR; (1) cured and discharged home, (2) cured and hospitalized, (3) cured and hospitalized with renal failure, (4) not cured, (5) dead) were used. DOOR is a recently developed statistical approach designed to unify important patient and clinician outcomes. Inverse probability of treatment weighted (IPTW) ordered logistic regression was used to model the odds of moving down ranked DOOR categories (i.e., having a worse outcome). The probability of a patient treated with CZA or a PBR having a worse DOOR category was also calculated. IPTW logistic regression was used to model the odds of 14-day mortality.

Results. 43 patients (CZA, n = 24; PBR, *n* = 19) with similar demographics and relative illness were included. *Klebsiella pneumoniae* (*n* = 21) and *Escherichia coli* (*n* = 16) were most common. 16/43 (37%) were CP CRE, 19/43 (44%) were non-CP CRE, and the remainder were unknown. The probability of a better DOOR for patients treated with CZA was 58% (95% CI 53% - 62%). Patients treated with CZA had an 81% reduction in IPTW-adjusted odds of a worse DOOR (OR 0.19, 95% CI 0.05 – 0.76; *P* = 0.02). 14-day mortality was 2/24 (8%) for patients receiving CZA vs. 5/19 (26%) for patients treated with PBR (IPTW-adjusted OR 0.12, 95% CI 0.02 – 0.82, P = 0.03).

Conclusion. These data suggest that CZA-based treatment, compared with PBR, has a superior integrated benefit-risk profile for the treatment of CRE bacteremia in cancer patients with a high burden of non-CP CRE. These findings build upon available data and suggest that CZA is preferred to PBR for CRE with heterogenous resistance mechanisms.

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2247. Real-world Experience with Meropenem–Vaborbactam (M/V) for Treatment of Carbapenem-Resistant Enterobacteriaceae (CRE) Infections

Ryan K. Shields, PharmD, MS[1]; Erin K. McCreary, PharmD, BCPS, BCIDP[2];
Rachel V. Marini, PharmD[3]; Ellen G. Kline, MS[4]; Chelsea E. Jones, BA[1];
Binghua Hao, MD, PhD[1]; Cornelius J. Clancy, MD[1]; Minh-Hong Nguyen, MD[1];
[1]University of Pittsburgh, Pittsburgh, Pennsylvania; [2]University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania; [3]UPMC Presbyterian, Pittsburgh, Pennsylvania; [4]University of Pittsburgh, School of Medicine, Pittsburgh, Pennsylvania

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Background. M/V demonstrates *in vitro* activity against KPC-producing CRE, but real-world clinical experience is limited.

Methods. Patients treated for > 48 hours with M/V for CRE infections were included. Success was defined as improved symptoms, absence of recurrent infection, and survival at 30 days. Microbiologic failures (MF) were defined as isolation of

the same species post-treatment (tx). KPC and *ompK36* mutations were detected by sequencing of PCR products.

Results. 19 patients were included; 58% were men; median age was 53. 11% were transplant recipients and median Charlson score was 3 (range: 0–10). Infection types included bacteremia (*n* = 7), pneumonia (6; 5 ventilator-associated), soft tissue (2), tracheobronchitis (2), intra-abdominal (1), and pyelonephritis (1). 68% of patients were in the ICU; median APACHE II and SOFA scores were 18 (7–40) and 4 (1–13), respectively. CR pathogens included *K. pneumoniae* (14), *K. oxytoca* (2), *E. coli* (2), and *C. freundii* (1); 89% harbored KPC, including KPC-2 (6), KPC-3 (10), and KPC-3 with a D179Y mutation (1). All were susceptible to M/V (median MIC = 0.03 µg/mL [0.015–0.12]). Median duration of tx was 8 days (3 – 28); 89% received monotherapy. Success and survival rates at 30d were 63% and 89%, respectively. Failures were due to death (2), recurrent infection (2), worse symptoms (2), and persistent bacteremia (1). Success rates for bacteremia and pneumonia were 57% and 67%, respectively. MF within 90 days occurred in 32% due to *K. pneumoniae* (5) or *E. coli* (1). MF were classified as intra-abdominal abscess (3), pneumonia (1), and respiratory (1) or urinary (1) colonization. The median time to MF was 32 days (15 – 67). M/V MICs were increased ≥8-fold against 67% (4/6) of recurrent isolates. 1 pt developed intra-abdominal infection due to M/V non-susceptible KPC-3 *K. pneumoniae* isolate (MIC = 8) following a 12-day of M/V; the recurrent isolate differed from the parent by an IS*5* insertion in the *ompK36* gene promoter. M/V was well-tolerated, 1 patient developed eosinophilia.

Conclusion. In this cohort of critically-ill patients with CRE infection, tx with M/V yielded outcomes comparable to prior cohorts treated with ceftazidime–avibactam. M/V non-susceptibility emerged in 1 isolate. Our findings require validation in future studies.

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2248. Clinical and Microbiological Outcomes Associated with Real-World Use of Ceftolozane/Tazobactam

Nicolo Cabrera, MD[1]; Truc T. Tran, PharmD[2]; William R. Miller, MD [2];
An Q. Dinh, BS[2]; Blake Hanson, PhD[3]; Jose M. Munita, MD[4];
Samuel A. Shelburne, MD, PhD[5]; Samuel A. Shelburne, MD, PhD[5];
Samuel L. Aitken, PharmD[5]; Samuel L. Aitken, PharmD[5];
Kevin W. Garey, PharmD, MS, FASHP[6]; Laura A. Puzniak, PhD[7];
Cesar A. Arias, MD, MSc, PhD, FIDSA[8]; [1]University of Texas Health Science Center at Houston, Houston, Texas; [2]Center for Antimicrobial Resistance and Microbial Genomics, UTHealth, Houston, Texas, Houston, Texas; [3]University of Texas Health Science Center School of Public Health, Houston, Texas; [4]Genomics and Resistant Microbes (GeRM) Group. Millennium Initiative for Collaborative Research On Bacterial Resistance (MICROB-R), Santiago, Region Metropolitana, Chile; [5]The University of Texas MD Anderson Cancer Center, Houston, Texas; [6]University of Houston College of Pharmacy, Houston, Texas; [7]Merck & Co., Inc., Kenilworth, New Jersey; [8]CARMiG, UTHealth and Center for Infectious Diseases, UTHealth School of Public Health, HOU, Texas; Molecular Genetics and Antimicrobial Resistance Unit and International Center for Microbial Genomics, Universidad El Bosque, BOG, COL, Houston, Texas

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Background. Ceftolozane/tazobactam (C/T) is a novel cephalosporin/β-lactamase inhibitor combination for treating Gram-negative infections, particularly Pseudomonas aeruginosa (PA). C/T has been FDA-approved for complicated intra-abdominal and urinary tract infections and has just completed a trial in ventilator nosocomial pneumonia, but real-world outcome data are still emerging.

Methods. Demographic, microbiologic, treatment and outcome data of patients who received C/T for ≥48 hours from January 2016 to August 2018 at multiple centers within a single hospital system were retrospectively collected. Available isolates were analyzed for C/T susceptibility (by Etest) and whole-genome sequencing (WGS). Spades v.3.11.1 was used for assembly, multi-locus sequence typing v2.10 performed for in silico MLST with the PubMLST database and Abricate v0.7 was used for resistance gene screening with the CARD database.

Results. Among 45 patients, 58% were non-white, 53% were female and 13% were immunocompromised. The median age was 64 years (IQR, 50 to 69). At the time of the index event, a high proportion of patients required ICU care (42%) and pressor support (13%) as well as had invasive devices in place (64%). A minority (2.4%) had prior exposure to C/T. Respiratory infections were most common (38%) followed by urinary tract (20%). Concomitant Gram-negative agents were used in 18%. 69% achieved clinical success (i.e., recovery from infection-related signs and symptoms). The in-hospital mortality rate was 16% of which 5 out of 7 were attributed to infection. Microbiology was available for 91% of patients; 84% had PA isolates resistant to at least 3 antipseudomonal classes (Figures 1 and 2). Ten PA isolates were analyzed with WGS (Table 1). C/T resistance arose during therapy in one patient (MIC increase from 1 to 128 µg/mL). WGS showed a substitution in AmpC β-lactamase (A46D) and presence of *blaCARB-2*.

Conclusion. Although C/T was used in a critically ill population with highly resistant organisms, cure rates were high and mortality was low. Acquired β-lactamases were not frequently seen among the PA isolates. C/T is a vital therapeutic option, particularly on MDR isolates for which options are limited.

Table 1 Whole genome sequence analysis of 10 *P. aeruginosa* isolates collected from patients receiving C/T

Isolate No.	Date of collection*	Source	C/T MIC (µg/ml)	ST	aminoglycoside resistance	β-lactamase	Other
1	-2	respiratory	0.75	novel	*aph(3')-IIb*		*catB7, fosA*
2	-3	blood	0.5	308	*aph(3')-IIb*		*catB7, fosA*
3	-8	wound	1	novel	*aph(3')-IIb*		*catB7, fosA*
4	0	respiratory	1.5	235	*aph(3')-IIb*	*bla*OXA-2	*catB7, fosA*
5	-5	respiratory	1.5	235	*aph(3')-IIb*		*catB7, fosA*
6	21	drainage	128	111	*aph(3')-IIb*	*bla*CARB-2, AmpCA46D	*catB7, fosA*
7	-2	biopsy	3	532	*aph(3')-IIb*		*catB7, fosA*
8	-9	respiratory	1.5	novel	*aph(3')-IIb*	*bla*OXA-2	*catB7, fosA*
9	-3	tissue	0.75	novel	*aph(3')-IIb*		*catB7, fosA*
10	-22	respiratory	4	novel	*aph(3')-IIb*		*catB7, fosA*

C/T - ceftolozane/tazobactam, MIC - minimum inhibitory concentration, ST - sequence type as determined by MLST
* day 0 is start date of C/T therapy