END OF STUDY

END OF STUDY

Aim…

In this section we will be considering the following…

- What does the ‘end of study’ mean?
- The number of ways that a patient can reach this point, planned, unplanned and when a trial closes
- How do protocols identify the pathway for patients when they come to the end of the study.
- What data is required and how often is follow up done, and for how long (signposts)
- ‘Monitoring, close out visits and regulatory documentation’, where does all the stuff go?
- Archiving
- How does the end of a study impact on the patient and their expectations; how are the family effected, how can we support the patients through this time, when do the nurses let go?

End of study defined…

- “The end-of-study is defined as the date of the last subject's last visit. The sponsor may also end the study upon confirmation that the primary endpoint was statistically met”

- The study may terminate prematurely, either in its entirety or at any study site, for reasonable cause; by the study team or by the investigator. The study may be stopped due to safety concerns, or because the trial drug has been deemed ineffective.

- We may determine the end of study as when a patient comes to the end of their time on the study,

Whatever the definition is behind the ‘end of study’, there will be systems created regarding the follow up of patients. There are 2 types of end of study, planned and unplanned

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The number of ways that a patient can reach this point, planned, unplanned and when a trial closes

Planned

- All studies have a start, a middle and an end; the expected end of study is determined at the beginning, this could be…
  - when the trial has met recruitment figures
  - when a patient has completed all the expected treatments and trial visits

Unplanned

- What quantifies an unplanned end of study?
  - If the patient withdraws
  - If the patient is unable to continue due to toxicities
  - If the patient becomes too unwell to continue
  - If the patient is non compliant
  - If the study closes due to safety issues

When a trial closes

- Once recruitment figures are met. Once a trial nears the completion of recruitment, sites are usually notified of limited slot availability. This is managed with effective communication (usually!)
- Trials can close if interim analysis finds unsatisfactory results, or if recruitment does not meet targets
- Patients who are on treatment after a trial has closed can sometimes continue on the IMP in a compassionate setting

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How do protocols identify the pathway for patients when they come to the end of the study?

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What data is required and how often is follow-up done and for how long…

Information from tables…

- The following tables show what end of study data collection is required…

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Activity	SCR	Cycle 1 Day –2	Cycle 1 Day 1	Cycle 1 Day 15	Cycle 2 – 6 Day 1	Final Visit	30-day FU Visit	Maintenance Therapy	Post-Treatment Visits	Survival Period
Informed Consent	X									
Medical and Cancer History	X									
Physical Exam (including weight)	X	X		X	X	X	X	X	X	
Vital Signs	X	X		X	X	X	X	X	X	
12-Lead ECG	X	X		X	X	X	X	X	X	
Performance Status (ECOG)	X	X		X	X	X	X	X	X	
Chemistry/Hematology	X	X		X	X	X	X	X	X	
UrinalysIS	X					X				
aPTT, INR	X									
Tumor Assessments	X				X	X			X	
MRI of the Brain	X									
Adverse Event and Concomitant										
Medication Assessment	X	X		X	X	X	X	X	X	
Randomizationg		X								
Dispense IMP		X	X		X					
chemotherapy			X		X					
Administer maintenance treatment								X		
Survival										X

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Vital Signs	X	X		X	X	X	X	X	X	
12-Lead ECG	X	X		X	X	X	X	X	X	
Performance Status (ECOG)	X	X		X	X	X	X	X	X	
Chemistry/Hematology	X	X		X	X	X	X	X	X	
UrinalysIS	X					X				
aPTT, INR	X									
Tumor Assessments	X				X	X			X	
MRI of the Brain	X									
Adverse Event and Concomitant										
Medication Assessment	X	X		X	X	X	X	X	X	
Randomizationg		X								
Dispense IMP		X	X		X					
chemotherapy			X		X					
Administer maintenance treatment								X		
Survival										X

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Vital Signs	X	X		X	X	X	X	X	X	
12-Lead ECG	X	X		X	X	X	X	X	X	
Performance Status (ECOG)	X	X		X	X	X	X	X	X	
Chemistry/Hematology	X	X		X	X	X	X	X	X	
UrinalysIS	X					X				
aPTT, INR	X									
Tumor Assessments	X				X	X			X	
MRI of the Brain	X									
Adverse Event and Concomitant										
Medication Assessment	X	X		X	X	X	X	X	X	
Randomizationg		X								
Dispense IMP		X	X		X					
chemotherapy			X		X					
Administer maintenance treatment								X		
Survival										X

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12-Lead ECG	X	X		X	X	X	X	X	X	
Performance Status (ECOG)	X	X		X	X	X	X	X	X	
Chemistry/Hematology	X	X		X	X	X	X	X	X	
UrinalysIS	X					X				
aPTT, INR	X									
Tumor Assessments	X				X	X			X	
MRI of the Brain	X									
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Medication Assessment	X	X		X	X	X	X	X	X	
Randomizationg		X								
Dispense IMP		X	X		X					
chemotherapy			X		X					
Administer maintenance treatment								X		
Survival										X

Information from text…

- “Following treatment discontinuation, subjects will have post-treatment visits 9 weeks until one year after randomization, then 12 weeks until radiographic progression or death.”

- “Subjects no longer undergoing clinical assessments will have survival information reported at 2-month intervals (or as requested by sponsor to support data analysis)beginning at the last clinical assessment and continuing until the endpoint of death, the subject has become lost to follow-up, or xxxx terminates the study. If the subject withdraws from study follow-up, the study staff may use a public information source(such as county records) to obtain information about survival status only, as appropriate per local regulations.”

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Signposts…

Look at the information contained in the extracts taken from a commercial trial, detailing the expected procedures following a patient finishing on trial. From this information we are able to determine what exactly is required at the ‘end of study’

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Signposts…

- Firstly it points out that patients have right to withdraw from study at any time. If this happens, we need to know if the patient has withdrawn totally, or if they would be happy to participate in the study for the purpose of data collection
- The protocol gives specific reasons as to why a patient should be withdrawn
- We are directed as to whether the patient needs to replaced if withdrawn
- We are then directed to continue with assessments until disease progression
- The patients final visit is clearly identified, we are also advised on what procedures should be followed prior to commencing new treatments
- We are clear about the timing of the follow up
- We know to follow up if a discontinued patient has ongoing adverse events
- Survival follow up data is requested at 2 month intervals
- This study identifies the variations of study drug treatment and cessation
- The entire study discontinuation is also discussed

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Monitoring, close out visits and regulatory documentation…

Where does all the stuff go?

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- Once the last patient has completed the study, or if the study closes early as previously discussed a study comes to it's end. At this point communication with the trial team increases, all data entered gets scrutinised and queries increase, documentation gets checked and monitoring visits increase… the pressure is cranked up!!!
- Once the trial team are happy that all the t's are crossed and the I's are dotted, the communication diminishes, and finally the study can be closed out.
- A close out visit is organised by the trial team.
- Once this has happened, the PI signs off all the relevant documentation and the trial team give the authority for the trial to be archived. At this point we can start to delete the emails!!! Important communications are copied and filed in the site file prior to this time.

Archiving

- In brief, once we are given the go ahead, the study can be archived
- All the site files can be boxed up and prepared for storage.
- Pharmacy files and site files are usually co-located.
- The files need to be stored for a minimum of 15 years.
- Patient notes need to have a sticker identifying that the notes have to be stored for 15 years, as these are not usually co-located.
- SOPs are devised, directing research departments on correct archiving methods. (see example)

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End of Study Quiz…

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You need enough energy to confront all the problems throughout the course of a trial!

- Psychological stress
- Work related burnout
- What are the warning signs?
- Leading to job dissatisfaction, possibly impaired work performance – lost days at work
- Support you can access? Informal or formal system (structured form of intervention)
  - **Answer may be both – informal group support to discuss emotional burden and more structured intervention 1:1**
- Quite often the lead researchers will have started planning a trial to take the place of the one that is ending. There may be pressure to open and increase workload – is there appreciation for what takes place when opening – emotional burden and still invested in present study that is closing.

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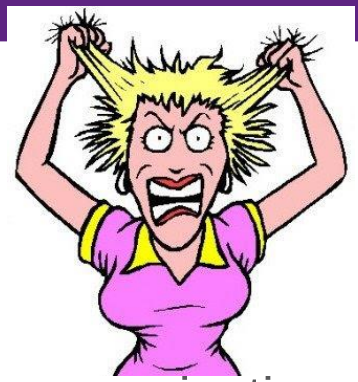
End of study, time



- Severity of the patients condition
- Increase in expectations of patient/family ?other members of the team
- Offering unsatisfactory care – may be few options for treatment
- Unable to control the results of the study
- Death of patients
- Problems related to family of patients
- Excessive job responsibility
- Problems of communication with team members
- Workload
- Problems with administrative systems
- Work conditions
- Lack of in service training
- No formal staff supervision
- New to speciality
- End of career
- Not feeling efforts appreciated

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Can you recognise serious stress?

- Staff who work as nurses, who were married, between 21 and 36, had work experience of 1-10 years, experienced conflict with colleagues, and who evaluated the fulfilment of job responsibilities, long and tiring work hours, lack of adequate material and tools and the problems experienced with patients and their relatives as stressful – found to have series job stress scores
  - ***Isikhan V Job stress and coping strategies in health care professionals working with cancer patients. European Journal of Oncology Nursing (2004) 8, 234-244***

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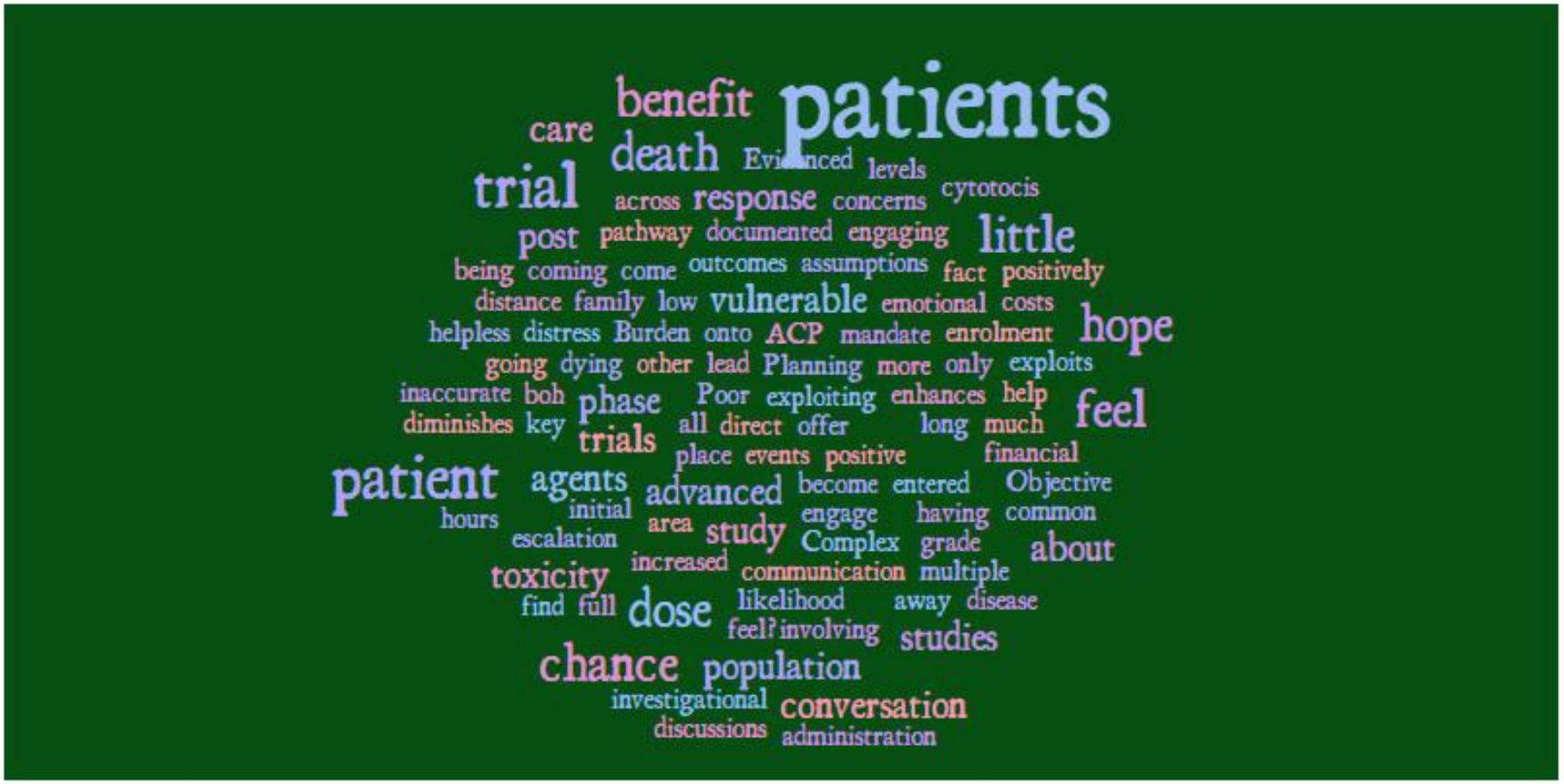
Letting go…



Top tips

- Communication – develop information packs for patients at end of study – where to go if unwell etc.
- Consent process discussion should include supportive care and prognosis
- Should not be early phase trial vs nothing – should have palliative care referral
- Evidence suggests that phase 1 patients vs palliative care patients have a different requirement from palliative care often wanting ‘practical’ help with transport, finances etc. they maintain hope for therapeutic benefit