From: Rivera, Donna (NIH/NCI) [F]

To: <u>Barbara M. Galligan</u>
Cc: <u>Benjamin Chan</u>

Subject: RE: SEER Data for NCI secondary malignancies

Date: Monday, June 27, 2016 3:45:30 PM

Attachments: sect 30 mds.pdf

sect 30 table.pdfsect 13 leu.pdfsect 13 table.08.pdf

Hi Barbara.

You are correct in that it is both under-reported and unavailable in SEER. The experts here said it is a project that is being work on. Here is an article describing the issues: http://www.time4epi.com/home/insights/time-for-an-epiphany/2014/04/22/mds-incidence-under-reported-and-under-diagnosed-

Barbara and Ben, here is what we have on MDS. You cannot use the analysis tool yet for MDS (like what I did for AML). Let me know what else I might be able to assist with (if we have it). The overall leukemia incidence charts are included as the incidence is higher and was not sure if that could help explain any of the issues. Thank you!

Sincerely, Donna

From: Barbara M. Galligan [mailto:bgalligan@ucdavis.edu]

Sent: Monday, June 27, 2016 12:45 PM

To: Benjamin Chan; Rivera, Donna (NIH/NCI) [F]

Subject: Re: SEER Data for NCI secondary malignancies

Sorry, Ben. MDS is a separate malignant hematologic disorder that can be a precursor to AML.

Adding the MDS data may help explain some of the numbers. It would be particularly helpful if SEER had:

de novo AML

secondary AML (secondary to hematologic disorder such as MDS) treatment related AML (often lumped in with "secondary")

but from Donna's last e-mail and other studies I've been reading it seems that is not available yet from SEER. Its difficult to tease out a de novo from a "secondary" AML even on a one-by-one basis let alone a population basis. You have to make assumptions based on the genetics of the AML.

Thanks you guys! Barbara

From: Benjamin Chan < chanb@ohsu.edu>
Sent: Monday, June 27, 2016 8:38:31 AM

To: 'Rivera, Donna (NIH/NCI) [F]'; Barbara M. Galligan

Subject: RE: SEER Data for NCI secondary malignancies

Oh, I assumed (incorrectly, it seems) that "AML" was a catch-all term for both. Yes, we should get MDS, to be comparable. Is that going to be a pain to get?

From: Rivera, Donna (NIH/NCI) [F] [mailto:donna.rivera@nih.gov]

Sent: Monday, June 27, 2016 6:37 AM **To:** Benjamin Chan; Barbara M. Galligan

Subject: RE: SEER Data for NCI secondary malignancies

I just wanted to make sure you saw the SEER statistics are only for AML and do not include MDS. MDS is categorized separately and we could get that as well for reference if you would like. There are other types such as AMoL and more rare versions ,if you would like to look at those. Let me know if there are other types needed for your reference.

From: Benjamin Chan [mailto:chanb@ohsu.edu]

Sent: Sunday, June 26, 2016 11:02 PM

To: Barbara M. Galligan < bgalligan@ucdavis.edu>; Rivera, Donna (NIH/NCI) [F]

<donna.rivera@nih.gov>

Subject: RE: SEER Data for NCI secondary malignancies

I'll take a closer look at the data to make sure I'm not doing something stupid, like counting a study twice or shifted a decimal one place over.

From: Barbara M. Galligan [bgalligan@ucdavis.edu]

Sent: Sunday, June 26, 2016 12:25 PM

To: Benjamin Chan; Rivera, Donna (NIH/NCI) [F]

Subject: Re: SEER Data for NCI secondary malignancies

Hi Ben & Donna,

The more I look at this the more our results are surprisingly high. It's also surprising that the taxanes are so significant. I've been surprised too that the anthracyclines are not significant.

A registry cohort from Sweedish in Seattle looking at MD/AML in BC patients and comparing with SEER data found a RR of MDS in pt age < 65 of 10.88 (95% CI 3.84,24.03) and a RR of AML in pt < 65 at 5.32 (95% CI 1.31, 14.04). No increased risk in pt > 65 or pts who did not receive radiation therapy.

Either we can really say something new! or we are missing something.

Barbara

From: Benjamin Chan < chanb@ohsu.edu > Sent: Saturday, June 25, 2016 8:01:11 AM

To: Rivera, Donna (NIH/NCI) [F]; Barbara M. Galligan Subject: RE: SEER Data for NCI secondary malignancies

Thanks, Donna.

BARBARA: it looks like the AML incidence is around 3.5-4.3 per 100,000 person-years from SEER.

From our data, I'm seeing about 54 per 100,000 p-y for low dose cyclophosphamide and 73 per 100,000 p-y for high dose. And 44 & 88 per 100,000 p-y for low- and high-dose taxane. Do those numbers match what you expected? They're really high compared to the SEER numbers.

```
drug x xHighDose malType predLin predBin scale
                         FALSE AML or MDS 54.88539 53.50585 1e+05
1: Cyclophosphamide 0.90
                         FALSE AML or MDS 56.86519 53.50585 1e+05
2: Cyclophosphamide 1.20
3: Cyclophosphamide 1.50
                         FALSE AML or MDS 58.91636 53.50585 1e+05
4: Cyclophosphamide 2.00
                         FALSE AML or MDS 62.50061 53.50585 1e+05
5: Cyclophosphamide 2.40
                         TRUE AML or MDS 65.52427 72.81951 1e+05
6: Cyclophosphamide 3.00
                         TRUE AML or MDS 70.33605 72.81951 1e+05
                         TRUE AML or MDS 75.50092 72.81951 1e+05
7: Cyclophosphamide 3.60
8: Cyclophosphamide 4.00
                         TRUE AML or MDS 79.15302 72.81951 1e+05
9: Cyclophosphamide 4.80
                         TRUE AML or MDS 86.99527 72.81951 1e+05
10: Cyclophosphamide 6.64
                          TRUE AML or MDS 108.10530 72.81951 1e+05
11: Cyclophosphamide 7.20
                          TRUE AML or MDS 115.49374 72.81951 1e+05
12: Cyclophosphamide 9.60
                          TRUE AML or MDS 153.31360 72.81951 1e+05
  drug x xHighDose malType predLin predBin scale
1: Taxane 3.0 FALSE AML or MDS 36.18930 43.80978 1e+05
2: Taxane 4.0 FALSE AML or MDS 43.77700 43.80978 1e+05
3: Taxane 4.5
             FALSE AML or MDS 48.14779 43.80978 1e+05
4: Taxane 6.0
              TRUE AML or MDS 64.05534 87.54615 1e+05
5: Taxane 7.0
              TRUE AML or MDS 77.48109 87.54615 1e+05
6: Taxane 8.0
              TRUE AML or MDS 93.71820 87.54615 1e+05
7: Taxane 9.0
              TRUE AML or MDS 113.35412 87.54615 1e+05
```

From: Rivera, Donna (NIH/NCI) [F] [donna.rivera@nih.gov]

Sent: Friday, June 24, 2016 7:24 AM

To: 'Barbara M. Galligan' Cc: Benjamin Chan

Subject: RE: SEER Data for NCI secondary malignancies

Hi Barbara.

I apologize for the delay in answering. I was out of the office. I am attaching a few options for types of analytic presentation for AML incidence. As for secondary malignancies, this is actually not easy to determine in SEER. There is a large amount of work around developing better algorithms for this. I have emailed the investigator working on secondary algorithms. Please let me know if these attached graphs (covering different years) are useful to you. There are several criteria I can apply to look at these in different ways or populations. Thank you!

Congrats on finishing up residency!!!!!! ③

Donna R. Rivera, PharmD., MSc.
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From: Barbara M. Galligan [mailto:bgalligan@ucdavis.edu]

Sent: Wednesday, June 22, 2016 2:10 PM

To: Benjamin Chan < chanb@ohsu.edu>; Rivera, Donna (NIH/NCI) [F] < donna.rivera@nih.gov>

Subject: Re: SEER Data for NCI secondary malignancies

Hi Donna,

Was wondering if you were able to make any progress finding somebody to help us get the SEER data for secondary malignancies? Thanks!

Barbara

From: Barbara M. Galligan

Sent: Friday, June 3, 2016 3:07:21 PM

To: Benjamin Chan; 'Rivera, Donna (NIH/NCI) [F]' Subject: Re: SEER Data for NCI secondary malignancies

Hi,

Looks good, but one thing:

I think we do need the incidence of primary (de novo) and secondary AMLs (secondary to other cancers). We are trying to see if the incidence in our population is higher than de novo, so that would be helpful. Having the rate of secondary malignancies may help validate what we find.

Thanks!
Barbara

From: Benjamin Chan < chanb@ohsu.edu>>

Sent: Friday, June 3, 2016 10:23:04 AM

To: 'Rivera, Donna (NIH/NCI) [F]'; Barbara M. Galligan Subject: RE: SEER Data for NCI secondary malignancies

Hi Donna,

Barbara will probably chime in with different thoughts, but I'll take a stab at answering your questions. See below. Might want to hold off until Barbara responds.

From: Rivera, Donna (NIH/NCI) [F] [mailto:donna.rivera@nih.gov]

Sent: Friday, June 03, 2016 5:20 AM To: Barbara M. Galligan; Benjamin Chan

Subject: RE: SEER Data for NCI secondary malignancies

Hi Barbara,

Happy to see if I can assist on this. If you can tell me the years, I want to confirm:

· AML Incidence (years??)

[BC] 1990-current

o Do you need it by gender or age? [BC] Just females age 40 y/o and older

Difference in secondary versus primary AML? (incidence and/ or prevalence??)

[BC] Secondary AML, MDS, and AML+MDS combined. Don't need primary. Just need incidence.

If it is just this, I have the software on my computer and might be able to do it myself. Let me know! If you are going to ASCO, I might see you there ©

Thank you!

Sincerely, Donna

Donna R. Rivera, PharmD., MSc.

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From: Barbara M. Galligan [mailto:bgalligan@ucdavis.edu]

Sent: Wednesday, June 01, 2016 1:24 PM

To: Rivera, Donna (NIH/NCI) [F]; Benjamin Chan Subject: SEER Data for NCI secondary malignancies

Hi Donna,

Thank you for mentioning that you have a contact person who is familiar with SEER data for AML. We would
like to know the standard incidence of AML. We are trying to divide out secondary vs primary AML occurrences.
I think current incidence rate is sufficient. I'll let Ben comment if he needs something more specific for analysis.
Ben - years that we are covering?

Thanks,

Barbara Galligan