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February 25, 2014

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# Evaluation of a “Practically Significant Dose” Using NOCTS Data

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## Introduction

During the SEC Work Group meeting on September 26, 2013, there was a discussion regarding the establishment of a practically significant dose (PSD) that could be used to guide the evaluation of coworker models. The concept was that this dose could be used to test the significance of observed differences between coworker distributions for various strata<sup>1</sup>. After some discussion, it was decided that an appropriate value for a PSD might be 100 mrem. If one were to adopt 100 mrem as a PSD, however, an evaluation of the impact on the outcome of a claim, i.e. the effect of probability of causation (PC), needed to be conducted.

## Description of the Evaluation

Given the large number of variables involved in the PC calculation, it would be very difficult (if not impossible) to generate hypothetical test cases that adequately test the impact of employing a 100 mrem significance threshold. NIOSH proposed, and the working group concurred, that the evaluation make use of the actual distribution of exposures and cancer scenarios contained in the approximately 40,000 claims in the NIOSH/OCAS Claims Tracking System (NOCTS) database. The approach that was adopted for this evaluation is described below.

- **Selection and characterization of the selected cases**

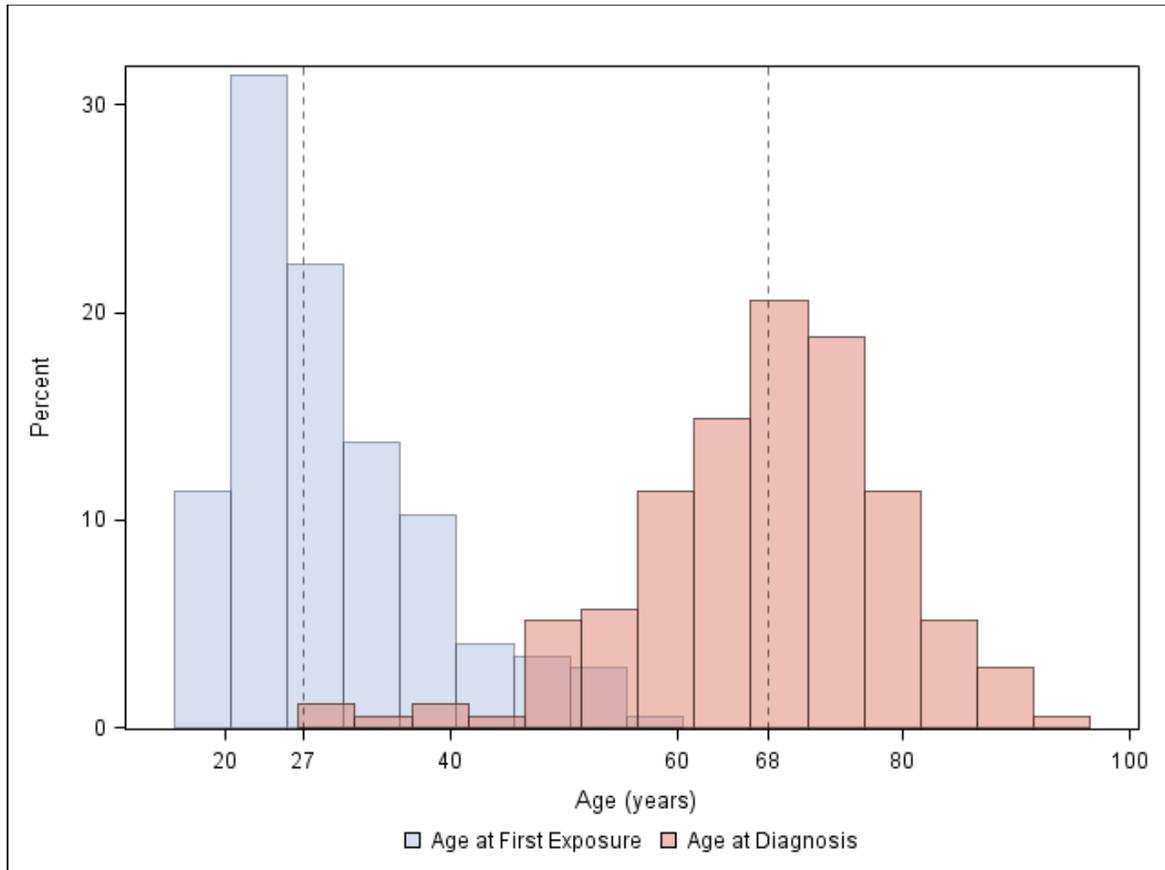
Claims with 99<sup>th</sup> percentile PC values between 45.00% and 49.99% were identified in the NOCTS database. As of October 29, 2013, 175 cases that met this criterion were identified out of the approximately 40,000 cases in the NOCTS database. The 175 selected cases corresponded to either claims having only one primary cancer, or to claims having more than one primary cancer, but with at least one of the primary cancers having a PC value between 45.00% and 49.99%. Only 25 out of the 33 available IREP cancer models are represented in the selected 175 cases. Almost one third of selected cases are represented by the Lung cancer (30.9%). Other cancer models with a large representation of cases are Non-melanoma BCC (16.6%), followed by All Male Genitalia (7.4%), Colon (6.3%), Lymphoma and multiple myeloma (5.7%), and Malignant melanoma (5.1%); each of the remaining cancer models contain less than 5% of the cases. The distribution of the cancer models represented in the 175 cases is provided in Table 1

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<sup>1</sup> It was also discussed that this dose might have other applications, such as in the evaluation of exposures during residual contamination periods.

of Attachment 1. The gender distribution of the cases is very close to the percentages of the gender distribution in the NOCTS database (i.e., approximately 90 percent males). As depicted in Figure 1 below, the median age at first exposure is 27 years and the median age at diagnosis is 68 years.

Figure 1: Distributions of the age of first exposure and the age of diagnosis.



All 175 cases were run on the IREP Enterprise Edition version at some point in the past, which means that the PC values on record, were generated based on 10,000 iterations and using a set of 30 different random seeds.

- **The scenarios evaluated**

In order to compare the effect of adding a 100 mrem dose to each of these cases, it was decided that three separate scenarios were required. The three scenarios, and the rationale behind each of them, are discussed below.

- 1) Scenario 1, also denoted as 'Original', corresponded to rerunning each case on the current IREP v.5.7 version. This was necessary because there have been several updates to the IREP models during the years, which might change the PC values slightly. The set of 30 random seeds that was originally used for each case were reused for the majority of the 175 cases.

For most of the 175 cases, the PC value obtained from Scenario 1 was the same as the original PC value recorded in the NOCTS database.

- 2) Scenario 2, also denoted as 'Add 0 mrem', corresponded to adding a constant dose of 0 mrem in each of the IREP files for the 175 cases. The 0 mrem was entered as an acute dose due to exposure from photons greater than 250 keV<sup>2</sup>. To ensure the effect of the cancer latency adjustment is minimized, the year of the additional exposure was selected differently for solid cancers versus leukemia cancers. For all solid cancers, and Chronic Lymphocytic Leukemia, the year corresponding to the additional 0 rem exposure was the first year of employment for each case. For all the leukemia cases, the year corresponding to the additional 0 rem exposure was 5 years before the diagnosis year, or the last year of employment (for those cases when the diagnosis year is more than five years after the last year of employment).
- 3) Scenario 3, also denoted as 'Add 100 mrem', corresponded to adding a constant dose of 100 mrem to each of the IREP files for the 175 cases. Similar to Scenario 2, the 100 mrem dose was entered as an acute dose, due to exposure from photons greater than 250 keV. The employment year where this additional exposure was added is the same as that described for Scenario 2.

- **Processing the case scenarios**

All 175 cases were run on IREP Enterprise Edition v.5.7, for each of the three scenarios described above. For each case, the three dose scenarios were run at 10,000 iterations using the same set of 30 random seeds. The same set of 30 random seeds was used to minimize the statistical uncertainty associated with the Monte Carlo sampling. In this way, the effect of only the added dose could be quantified. However, as will be explained in more detail later, even though all three scenarios use the same set of 30 random seeds, the addition of a new exposure line in Scenarios 2 and 3 altered the sequence of random numbers as compared to Scenario 1. Because of this, only Scenarios 2 and 3 use the exact same set of random numbers in the process of computing the PC values.

- **Comparison of the results**

After running all the 175 cases on IREP Enterprise Edition v.5.7 for each of the three dose scenarios described above, the average of the 99<sup>th</sup> percentile PC values from the 30 runs

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<sup>2</sup> The Radiation Effectiveness Factor (REF) for photons >250 keV is considered to be a constant. Thus, the outcome of any change in PC would be directly related to the additional dose and not influenced by the uncertainty in REF that is associated with lower energy photons.

(corresponding to the 30 different random seeds) was computed and recorded; these average PC values will be denoted from now on as Avg. PC values.

In order to determine the effect of adding the additional 100 mrem external dose to the existing dose for each case, the differences in the Avg. PC values were compared for each of the 175 cases, among the three dose scenarios. The comparison of interest is the Avg. PC values between Scenarios 2 and 3. Since these two scenarios use the exact the same set of random numbers during the computation of the PC values, this allows for a direct comparison of the effect of the added dose.

### Results of the evaluation

The summary statistics for the Avg. PC values from the three dose scenarios are shown in Table 1. While the 175 cases were initially selected to have a PC value between 45.00% and 49.99%, in the process of rerunning the cases on the current IREP version v5.7, some of the cases had a small change in the PC values, due to some of the updates that were implemented in the more recent IREP versions; as a result of this, two of the cases with lung cancer which had a small decrease in the PC values, had the Avg. PC values for Scenario 1 (Original) go slightly below the 45.00% threshold. The Avg. PC values obtained for each of the 175 cases, for each of three dose scenarios, are listed in Table 2 of Attachment 1. It is of interest to note that, after the addition of 100 mrem, not one of the 175 cases evaluated resulted in an Avg. PC value of greater than or equal to 50.00%.

Table 1: Summary statistics for the Avg. PC values from the three dose scenarios.

Dose Scenario	N	Min	Median	Mean	Max
Scenario 1 (Original)	175	44.93	47.43	47.38	49.87
Scenario 2 (Add 0 mrem)	175	44.73	47.39	47.38	49.90
Scenario 3 (Add 100 mrem)	175	44.92	47.44	47.45	49.92

The summary statistics for the Avg. PC values from the three dose scenarios, by cancer type are shown in Table 2. The leukemia cancers (excl. CLL) contain 2 cases with the 'Acute Myeloid Leukemia' cancer model, and 3 cases with 'Leukemia (excl. CLL)' cancer model.

Table 2: Summary statistics for the Avg. PC values from the three dose scenarios, by cancer type.

Cancer Type	Dose Scenario	N	Min	Median	Mean	Max
Solid cancers, and CLL	Scenario 1 (Original)	170	44.93	47.47	47.38	49.87
	Scenario 2 (Add 0 mrem)	170	44.73	47.40	47.39	49.90
	Scenario 3 (Add 100 mrem)	170	44.92	47.43	47.44	49.92
Leukemia cancers (excl. CLL)	Scenario 1 (Original)	5	45.32	47.43	47.37	49.08
	Scenario 2 (Add 0 mrem)	5	45.16	47.37	47.31	49.09
	Scenario 3 (Add 100 mrem)	5	45.40	47.67	47.59	49.43

Table 3 shows the distribution of positive/negative/zero changes in the Avg. PC values, when comparing two of the three dose scenarios, side by side. For the main comparison, between Scenario 2 versus Scenario 3, 173 cases had an increase in the Avg. PC value, and 2 cases had no change in the Avg. PC values.

Table 3: Distribution of positive/negative/zero changes in the Avg. PC values among the scenarios evaluated.

<b>Change from Scenario 2 to Scenario 3</b>	<b>Frequency</b>	<b>Percent</b>
No change from Scenario 2 to Scenario 3	2	1.1
Positive change from Scenario 2 to Scenario 3	173	98.9
<b>Total</b>	<b>175</b>	<b>100.00</b>

<b>Change from Scenario 1 to Scenario 3</b>	<b>Frequency</b>	<b>Percent</b>
Negative change from Scenario 1 to Scenario 3	64	36.6
No change from Scenario 1 to Scenario 3	4	2.3
Positive change from Scenario 1 to Scenario 3	107	61.1
<b>Total</b>	<b>175</b>	<b>100.00</b>

<b>Change from Scenario 1 to Scenario 2</b>	<b>Frequency</b>	<b>Percent</b>
Negative change from Scenario 1 to Scenario 2	85	48.6
No change from Scenario 1 to Scenario 2	4	2.3
Positive change from Scenario 1 to Scenario 2	86	49.1
<b>Total</b>	<b>175</b>	<b>100.00</b>

The summary statistics for the differences in the Avg. PC from the three dose scenarios are shown in Table 4. The summary statistics for the differences in the Avg. PC from the three dose scenarios, by cancer type, are shown in Table 5.

Table 4: Summary statistics for the differences in Avg. PC values, between Scenario 3 vs. Scenario 1, and between Scenario 3 vs. Scenario 2.

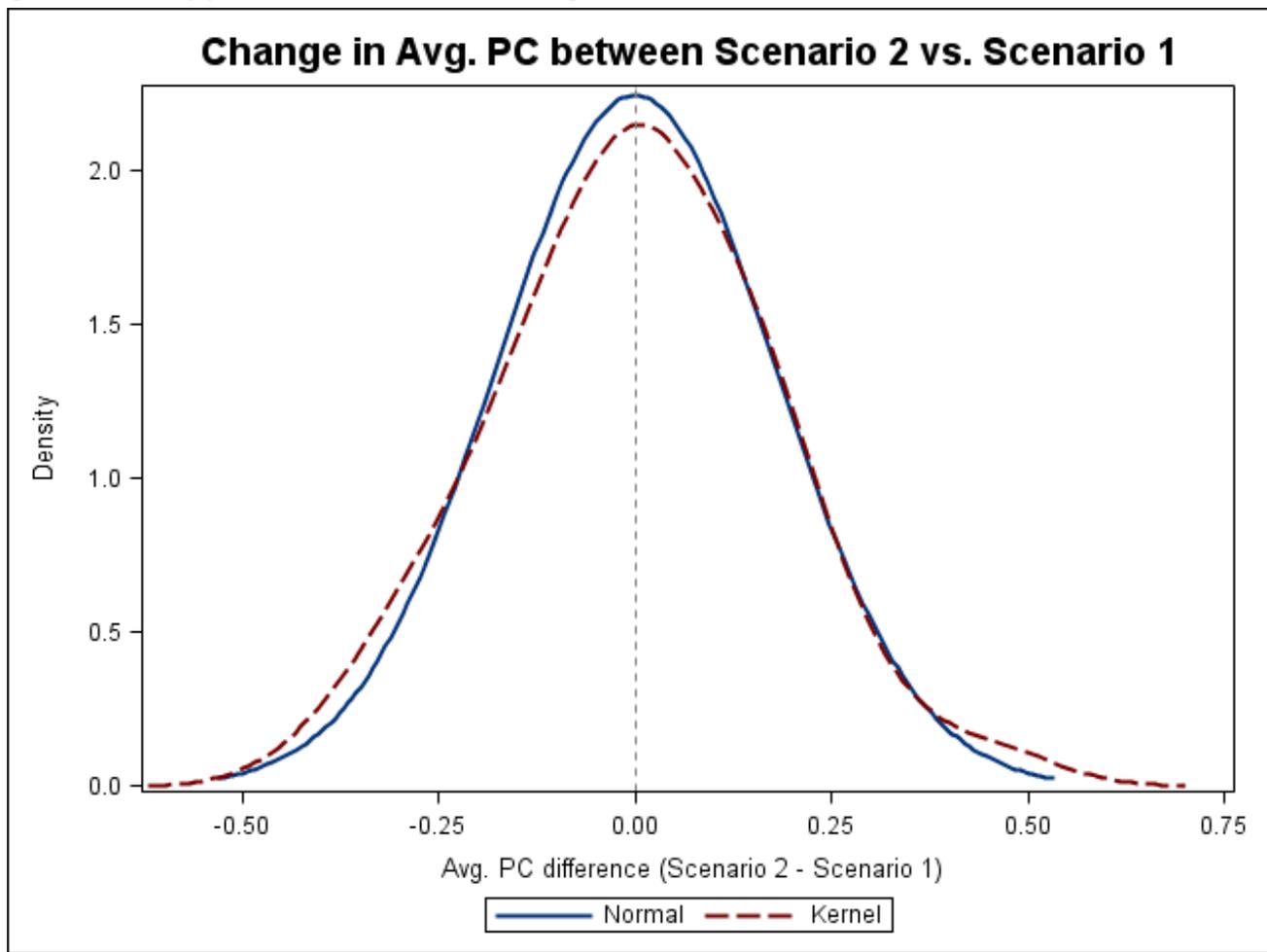
<b>Difference in Avg. PC values</b>	<b>N</b>	<b>Min</b>	<b>5<sup>th</sup> pctl.</b>	<b>Median</b>	<b>Mean</b>	<b>95<sup>th</sup> pctl.</b>	<b>Max</b>
Scenario 3 – Scenario 1	175	-0.43	-0.26	0.06	0.06	0.37	0.67
Scenario 3 – Scenario 2	175	0.00	0.01	0.02	0.06	0.25	0.34

Table 5: Summary statistics for the differences in Avg. PC values, by cancer type, between Scenario 3 vs. Scenario 1, and between Scenario 3 vs. Scenario 2.

<b>Cancer Type</b>	<b>Difference in Avg. PC values</b>	<b>N</b>	<b>Min</b>	<b>Median</b>	<b>Mean</b>	<b>Max</b>
Solid cancers, and CLL	Scenario 3 – Scenario 1	170	-0.43	0.05	0.06	0.67
	Scenario 3 – Scenario 2	170	0.00	0.02	0.06	0.34
Leukemia cancers (excl. CLL)	Scenario 3 – Scenario 1	5	0.08	0.21	0.22	0.35
	Scenario 3 – Scenario 2	5	0.18	0.30	0.28	0.34

A density plot for the differences in Avg. PC values, between Scenario 2 vs. Scenario 1, is shown in Figure 2. The differences in the Avg. PC values between Scenario 2 vs. Scenario 1 are normally distributed around 0, with a standard deviation of 0.18. Since the total dose in Scenarios 1 and 2 is exactly the same, and the uncertainty around each individual dose is exactly the same, the only factor that affect the differences in the Avg. PC values between these two scenarios, is the different sequence of random numbers that is used in generating the PC values. The reason for the different sequences of random numbers is due to the fact that Scenario 2 has one additional exposure than Scenario 1 (an additional exposure of 0 mrem is added to the IREP file in Scenario 2), which has the effect that an additional set of ERR (Excess Relative Risk) values is allocated by IREP for this additional exposure. This extra set of ERR values will use the next 10,000 random numbers in the sampling sequence, and this will have the effect of using a different set of random numbers for all the remaining computations. The final effect is that Scenario 2 is equivalent to running the same IREP file as in Scenario 1, but with a different set of 30 random seeds.

Figure 2: Density plot for the differences in Avg. PC values, between Scenario 2 vs. Scenario 1.



Boxplots with the differences in Avg. PC values, between Scenario 3 vs. Scenario 1, and between Scenario 3 vs. Scenario 2, are shown in Figures 3 and 4. These two boxplots show the first quartile, the median, and the third quartile of these distributions, while the whiskers of each boxplot extend to the extreme values of the corresponding distributions; the diamond symbol in each boxplot represents the mean value of the distribution.

For our comparison of interest, between Scenario 3 vs. Scenario 2, the difference in the Avg. PC values between the two dose scenarios is between 0 and 0.34, with a median value of 0.02, and a mean value of 0.06. The middle 50% of the differences in the Avg. PC between Scenario 3 vs. Scenario 2, are between 0.02 and 0.08, and the middle 90% of the differences in the Avg. PC are contained between 0.01 and 0.25. The largest increase of 0.34 in the Avg. PC values occur for three cases, with Leukemia (excl. CLL), Acute Myeloid Leukemia, and Non-melanoma BCC cancers; the next largest increases of 0.31 and 0.30 also occur for the Non-melanoma BCC, and Acute Myeloid Leukemia cases. The two cases where there was no increase in the Avg. PC values have the same cancer model, Oral Cavity and Pharynx.

Figure 3: Boxplot for the differences in Avg. PC values, between Scenario 3 vs. Scenario 1.

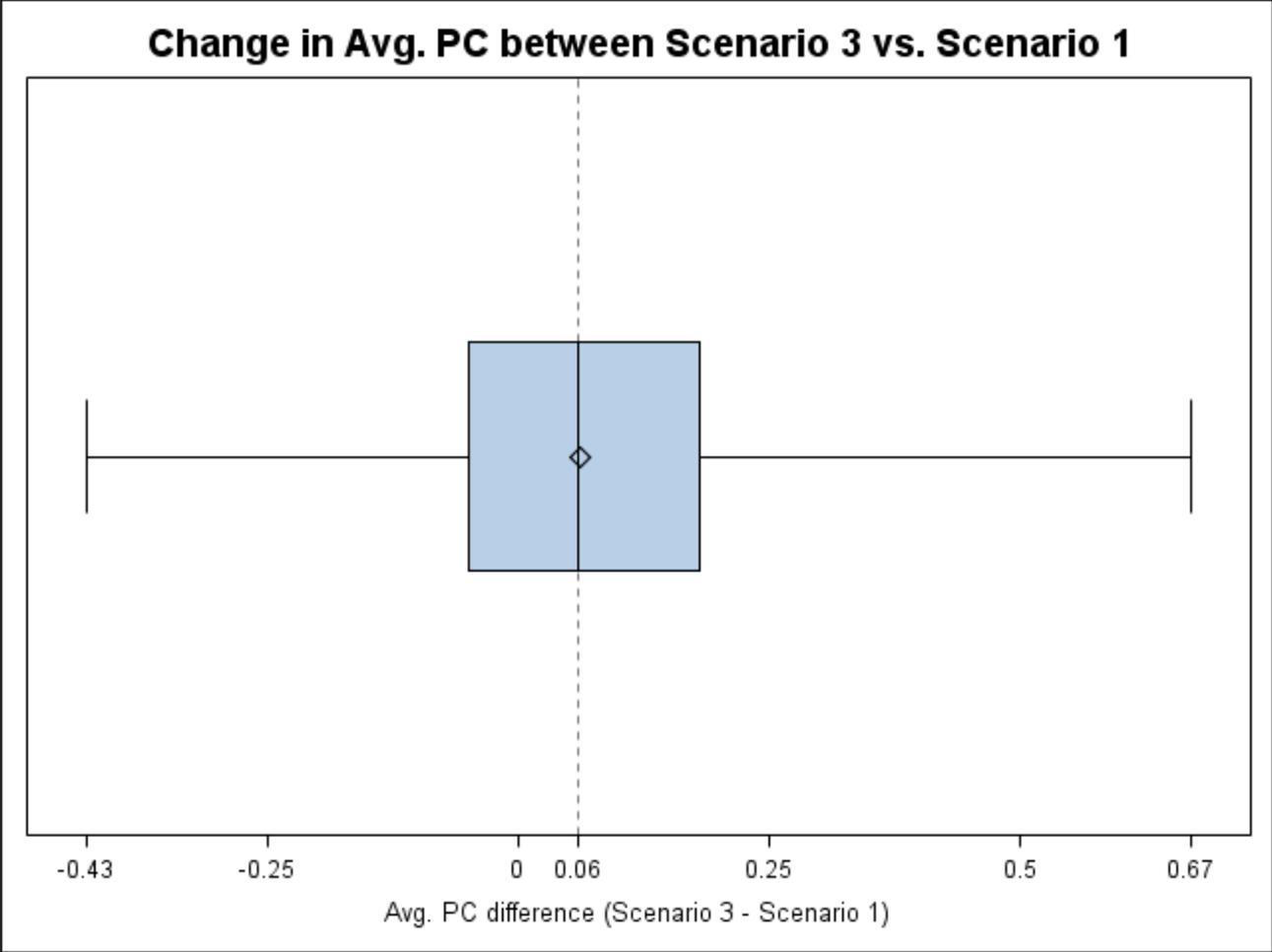
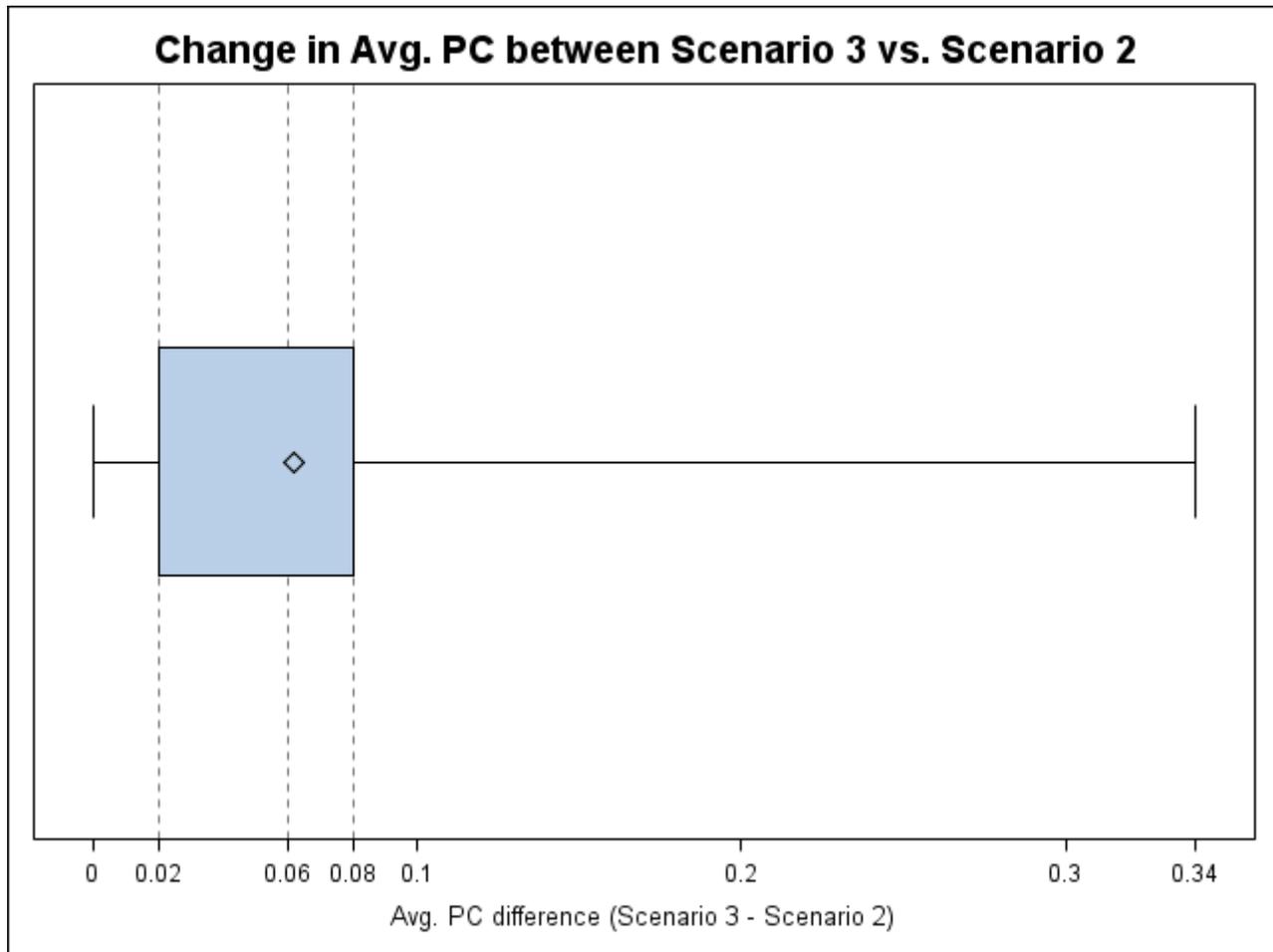
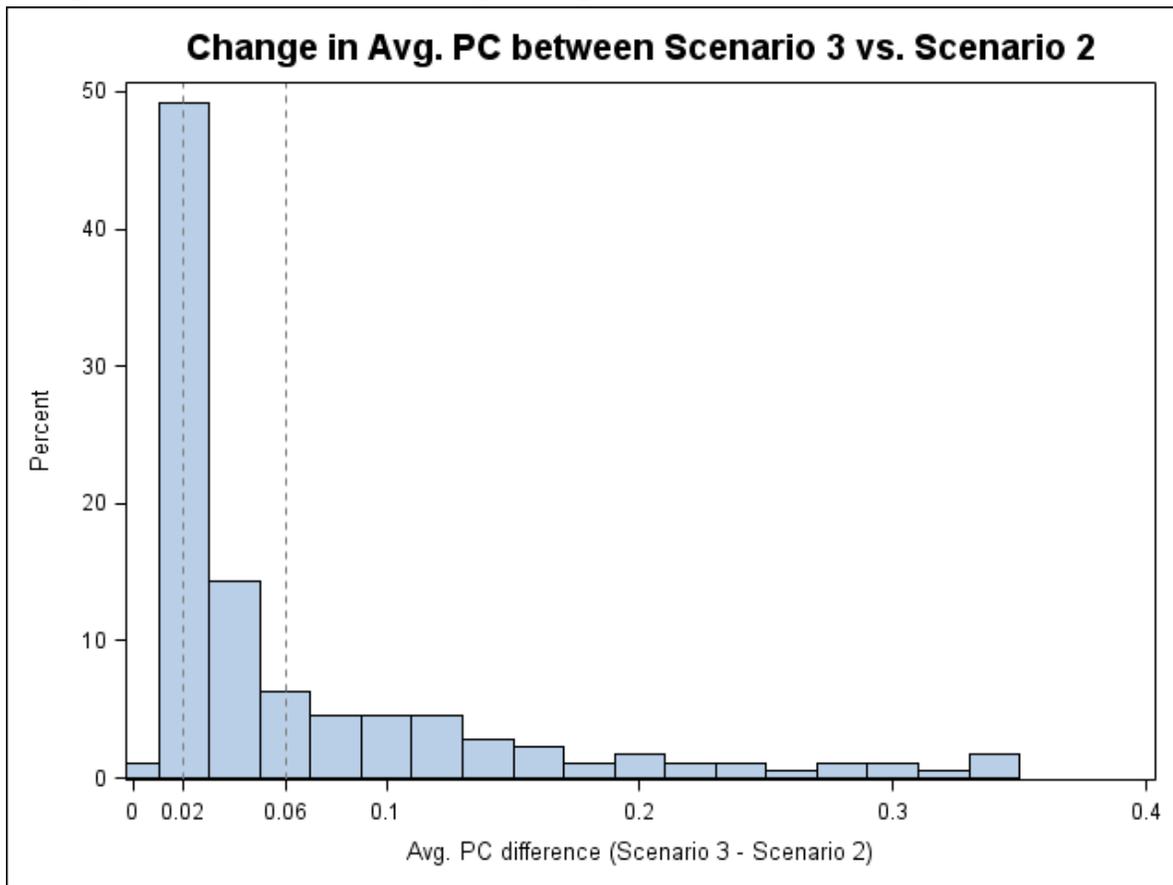


Figure 4: Boxplot for the differences in Avg. PC values, between Scenario 3 vs. Scenario 2.



A histogram that shows the distribution in the difference of Avg. PC value between Scenarios 3 and 2 is provided in Figure 5. Unlike the values in Figure 2 which are normally distributed around zero (standard deviation = 0.18), the values in Figure 5 are log-normally distributed with a median value 0.02. Because both Scenarios 2 and 3 were run using the same sequence of random numbers, the observed differences were solely due to the additional excess relative risk that was imparted due to the added dose. In fact, the majority of observed spread of the differences in PC is due to the differences in radiosensitivity associated with the various cancer models.

Figure 5: Distribution of the change in Avg. PC values with the addition of 100 mrem.



Attachment 2 includes side-by-side boxplots for the 99<sup>th</sup> percentile PC values from the three dose scenarios, for each of the 175 cases. These boxplots show the distribution of the 99<sup>th</sup> percentile PC values, corresponding to the sets of 30 random seeds used for each case. Each of these boxplots shows the first quartile, the median, and the third quartile of these distributions, while the whiskers from each boxplot extend to the 5<sup>th</sup> and 95<sup>th</sup> percentiles of the distributions. The Avg. PC values (which are also listed in Table 2 of Attachment 1) are displayed as small circles in these boxplots. The 175 cases are displayed in separate plots, which are grouped by the 25 IREP cancer models.

These side-by-side boxplots show a pretty clear picture that the results from the three dose scenarios for each case have not only very close Avg. PC values, but the distributions of the PC values is very similar across the three dose scenarios and almost identical for Scenario 2 versus Scenario 3, for most of the cases.

## Conclusion

An evaluation was designed to determine the effect of adding an additional 100 mrem external dose to the cases from NOCTS database, with PC values between 45.00% and 49.99%. Three different dose scenarios were used for each of the 175 cases selected for this experiment: Scenario 1 (also denoted as 'Original'), Scenario 2 (also denoted as 'Add 0 mrem'), and Scenario 3 (also denoted as 'Add 100 mrem'). Comparing the results from Scenario 1 versus Scenario 3 doesn't really show the true effect of adding the additional 100 mrem dose, since the two dose scenarios do not use the exact same sequence of random numbers in order to generate the Avg. PC values. In order to eliminate the random noise associated with choosing a different set of random numbers in the process of computing the PC values, our main focus was the comparison between Scenario 2 and Scenario 3, which allows for a direct comparison of the effect of adding the 100 mrem dose to the existing dose for each case.

After running each case on the different dose scenarios, it was observed that for each of the 175 cases, the Avg. PC values from Scenario 3 is greater than or equal to the Avg. PC from Scenario 2, as was expected. However, the increase in the Avg. PC results from these two scenarios is small, with a range between the two dose scenarios from 0 to 0.34, with a median increase of 0.02, and a mean increase of 0.06. The largest increases occur for the leukemia cancer claims, which may be related to the relative radiosensitivity of blood forming organs over other tissue types. It was also observed that 90% of the increase in the Avg. PC values between Scenario 2 and Scenario 3 are contained between 0.01 and 0.25.

## Attachment 1

Table 1: IREP cancer models for the 175 selected cases.

IREP Cancer Model	Frequency	Percent
Acute Myeloid Leukemia	2	1.1
All Male Genitalia	13	7.4
Bladder	4	2.3
Bone	2	1.1
Chronic Lymphocytic Leukemia	1	0.6
Colon	11	6.3
Connective tissue	1	0.6
Gallbladder	4	2.3
Leukemia (excl. CLL)	3	1.7
Liver	1	0.6
Lung	54	30.9
Lymphoma and multiple myeloma	10	5.7
Malignant melanoma	9	5.1
Nervous system	3	1.7
Non-melanoma BCC	29	16.6
Non-melanoma SCC	2	1.1
Oral Cavity and Pharynx	2	1.1
Other and ill-defined sites	2	1.1
Other respiratory	1	0.6
Ovary	1	0.6
Pancreas	2	1.1
Rectum	1	0.6
Stomach	8	4.6
Thyroid	3	1.7
Urinary organs (excl. bladder)	6	3.4
<b>Total</b>	<b>175</b>	<b>100.0</b>

**Table 2: Avg. PC results from the scenarios evaluated for the 175 selected cases**

Claim	IREP Cancer Model	Avg. PC (Original)	Avg. PC (Add 0 mrem)	Avg. PC (Add 100 mrem)		Claim	IREP Cancer Model	Avg. PC (Original)	Avg. PC (Add 0 mrem)	Avg. PC (Add 100 mrem)
1	Lung	44.93	45.16	45.17		32	Gallbladder	49.05	49.20	49.27
2	Lung	45.86	46.06	46.07		33	Non-melanoma BCC	45.21	45.22	45.37
3	Lung	46.52	46.57	46.61		34	Lung	45.94	45.97	45.99
4	Pancreas	47.11	47.08	47.10		35	Colon	46.66	46.59	46.64
5	Lung	47.71	47.76	47.77		36	Malignant melanoma	47.28	47.07	47.18
6	All Male Genitalia	48.28	48.31	48.33		37	Stomach	47.85	47.81	47.90
7	Malignant melanoma	45.08	44.73	44.92		38	Lung	48.42	48.45	48.46
8	Non-melanoma BCC	45.91	46.43	46.58		39	Leukemia (excl. CLL)	49.08	49.09	49.43
9	Malignant melanoma	46.52	46.50	46.63		40	Non-melanoma BCC	45.23	45.17	45.23
10	Lung	47.15	47.02	47.04		41	Oral Cavity and Pharynx	45.98	46.16	46.16
11	Non-melanoma BCC	47.74	47.59	47.72		42	Non-melanoma BCC	46.72	46.68	46.89
12	Lung	48.30	48.47	48.49		43	Thyroid	47.85	48.01	48.28
13	Non-melanoma BCC	48.88	48.79	48.91		44	Lymph. and mult. myel.	48.42	48.53	48.55
14	Non-melanoma BCC	45.13	45.32	45.41		45	Lung	49.08	48.97	49.07
15	Lung	45.90	45.76	45.80		46	Lung	45.24	45.34	45.47
16	Connective tissue	46.53	46.36	46.41		47	Non-melanoma BCC	46.81	46.72	46.78
17	Non-melanoma BCC	47.15	47.00	47.11		48	Malignant melanoma	47.33	47.03	47.11
18	Stomach	47.80	47.94	47.98		49	Lung	47.89	47.60	47.61
19	Lung	48.39	48.33	48.34		50	Lymphoma and multiple myeloma	48.42	48.84	48.86
20	All Male Genitalia	48.89	48.98	48.99		51	Lung	49.09	49.09	49.12
21	Lung	45.10	45.31	45.33		52	Non-melanoma BCC	45.31	45.37	45.71
22	Urinary organs (excl. bladder)	45.90	45.79	45.87		53	Colon	46.09	45.92	45.94
23	Non-melanoma BCC	46.53	46.52	46.69		54	Stomach	46.81	47.14	47.18
24	Bladder	47.18	47.32	47.34		55	Non-melanoma BCC	47.41	47.12	47.28
25	Lung	48.41	48.37	48.39		56	Non-melanoma BCC	47.94	48.11	48.17
26	Oral Cavity and Pharynx	48.69	48.94	48.94		57	Malignant melanoma	48.46	48.42	48.54
27	Non-melanoma BCC	45.17	45.08	45.13		58	Bladder	49.13	49.00	49.03
28	Malignant melanoma	45.91	45.82	45.93		59	Leukemia (excl. CLL)	45.32	45.16	45.40
29	Other and ill-defined sites	46.61	46.63	46.65		60	All Male Genitalia	46.11	45.93	45.95
30	Ovary	47.23	47.56	47.60		61	All Male Genitalia	46.82	46.90	46.91
31	Non-melanoma BCC	47.85	47.45	47.58		62	Colon	47.41	47.53	47.57

**Table 2: Avg. PC results from the scenarios evaluated for the 175 selected cases (continued)**

Claim	IREP Cancer Model	Avg. PC (Original)	Avg. PC (Add 0 mrem)	Avg. PC (Add 100 mrem)		Claim	IREP Cancer Model	Avg. PC (Original)	Avg. PC (Add 0 mrem)	Avg. PC (Add 100 mrem)
63	Acute Myeloid Leukemia	47.93	47.80	48.14		92	Non-melanoma BCC	45.43	45.35	45.54
64	Urinary organs (excl. bladder)	48.50	48.76	48.78		93	Nervous system	46.23	46.03	46.04
65	Lung	49.14	49.12	49.13		94	Lung	46.98	46.96	46.98
66	Lung	44.97	44.98	44.99		95	Stomach	47.51	47.34	47.39
67	All Male Genitalia	46.05	46.09	46.16		96	Lung	48.09	48.04	48.06
68	Colon	46.83	46.85	46.89		97	Non-melanoma BCC	48.66	48.43	48.74
69	Acute Myeloid Leukemia	47.43	47.37	47.67		98	Bladder	49.19	49.15	49.17
70	Lung	47.93	48.14	48.18		99	Bone	45.44	45.29	45.30
71	Chronic Lymphocytic Leukemia	48.52	48.43	48.45		100	Lung	46.24	46.33	46.35
72	Non-melanoma BCC	49.18	49.64	49.73		101	Thyroid	46.99	47.15	47.36
73	Lymphoma and multiple myeloma	45.33	45.07	45.08		102	Colon	47.53	47.55	47.58
74	Lung	46.13	46.12	46.13		103	Lymph. and mult. myel.	48.12	48.42	48.44
75	Lymphoma and multiple myeloma	46.92	46.99	47.02		104	Liver	48.66	48.81	48.90
76	All Male Genitalia	47.43	47.34	47.35		105	Other and ill-defined sites	49.36	49.35	49.37
77	Nervous system	47.99	47.89	47.90		106	Lymphoma and multiple myeloma	45.47	45.67	45.69
78	Lung	48.53	48.40	48.42		107	All Male Genitalia	46.31	46.46	46.49
79	Stomach	49.18	49.07	49.26		108	Malignant melanoma	47.00	46.65	46.77
80	Lymphoma and multiple myeloma	45.33	45.64	45.65		109	Lung	47.53	47.87	47.88
81	Colon	46.19	46.02	46.07		110	Lung	48.14	48.11	48.13
82	Lung	48.02	48.07	48.09		111	Lung	48.72	48.72	48.73
83	Lung	48.58	48.70	48.72		112	Non-melanoma BCC	49.38	49.46	49.61
84	Lung	49.22	49.26	49.27		113	Colon	45.49	45.57	45.60
85	Thyroid	45.33	45.41	45.64		114	Stomach	46.24	46.09	46.15
86	Lung	46.23	46.16	46.19		115	Colon	47.02	46.99	47.01
87	All Male Genitalia	46.98	46.72	46.74		116	Other respiratory	47.53	47.53	47.54
88	Lung	47.51	47.72	47.73		117	Colon	48.15	48.24	48.26
89	Malignant melanoma	48.08	48.15	48.28		118	All Male Genitalia	48.73	48.90	48.91
90	Bone	48.61	48.40	48.42		119	Urinary org. (excl. blad.)	49.44	49.62	49.64
91	Lung	49.23	49.19	49.20		120	Lung	45.50	45.19	45.20

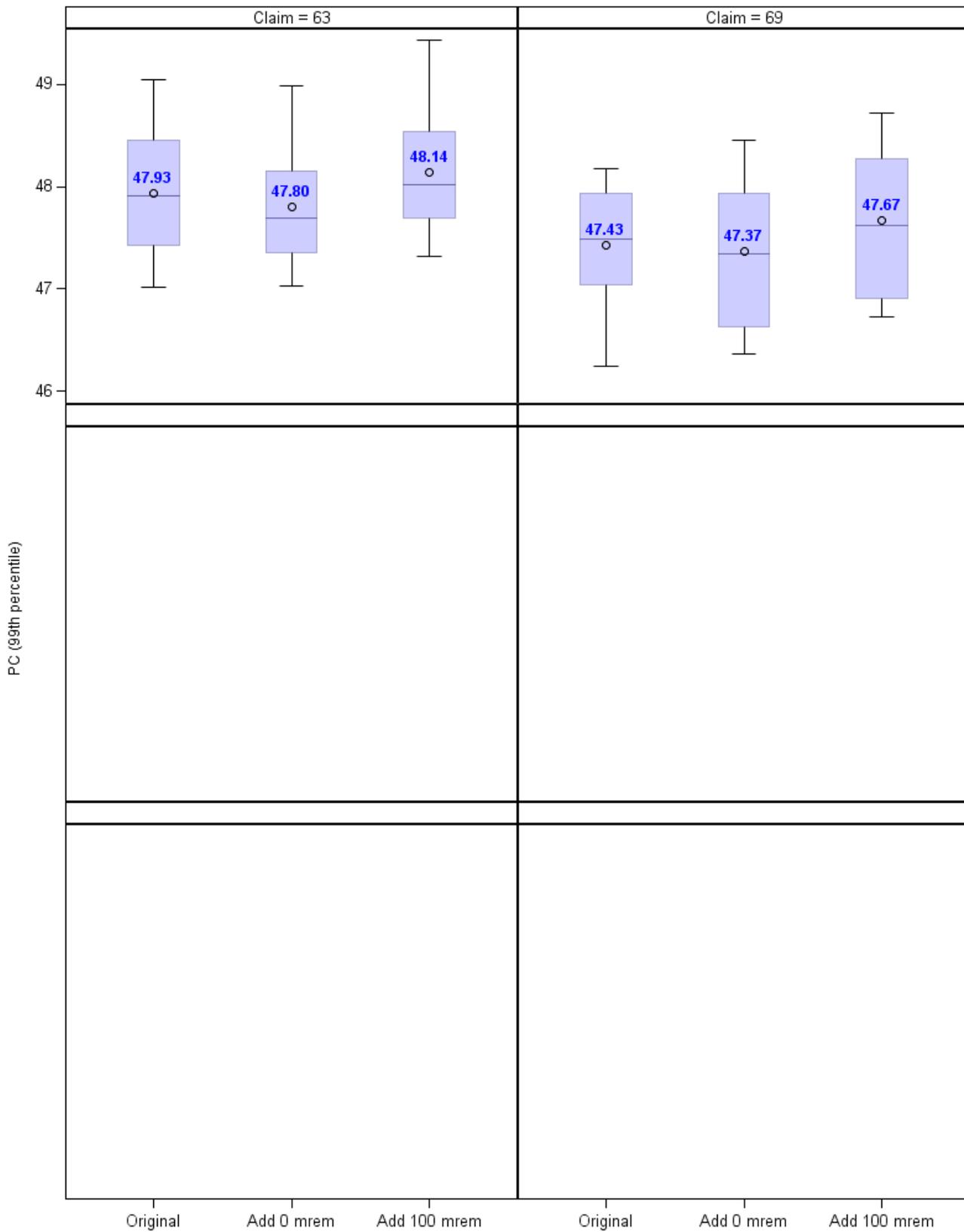
**Table 2: Avg. PC results from the scenarios evaluated for the 175 selected cases (continued)**

Claim	IREP Cancer Model	Avg. PC (Original)	Avg. PC (Add 0 mrem)	Avg. PC (Add 100 mrem)		Claim	IREP Cancer Model	Avg. PC (Original)	Avg. PC (Add 0 mrem)	Avg. PC (Add 100 mrem)
121	Malignant melanoma	46.33	46.42	46.50		150	Urinary organs (excl. bladder)	49.84	49.74	49.75
122	All Male Genitalia	47.04	46.74	46.76		151	Lung	45.24	45.68	45.73
123	All Male Genitalia	47.54	47.77	47.79		152	Colon	46.49	46.41	46.44
124	Lymphoma and multiple myeloma	48.15	47.71	47.72		153	Leukemia (excl. CLL)	47.10	47.13	47.31
125	Non-melanoma BCC	48.77	48.80	49.05		154	Non-melanoma BCC	47.72	47.95	48.04
126	Lung	49.57	49.82	49.84		155	Lung	48.27	48.27	48.31
127	Non-melanoma BCC	45.56	45.67	45.73		156	Lung	48.87	48.72	48.73
128	All Male Genitalia	46.44	46.37	46.39		157	Urinary organs (excl. bladder)	49.87	49.88	49.90
129	Bladder	47.06	47.22	47.24		158	Gallbladder	45.86	45.90	45.97
130	Lung	47.55	47.49	47.50		159	Non-melanoma BCC	46.49	46.48	46.59
131	Lung	48.38	48.53	48.55		160	Lung	47.11	46.86	46.89
132	Lung	48.81	48.75	48.76		161	Lung	47.71	47.31	47.32
133	Lung	45.41	45.13	45.15		162	Urinary organs (excl. bladder)	48.27	47.99	48.01
134	Lymphoma and multiple myeloma	46.46	46.45	46.46		163	Non-melanoma BCC	48.87	48.92	49.19
135	Colon	47.06	46.92	46.95		164	Lung	49.36	49.54	49.55
136	Lung	47.57	47.39	47.41		165	Non-melanoma BCC	48.88	48.92	49.02
137	Non-melanoma BCC	48.24	48.35	48.42		166	Rectum	47.83	48.00	48.01
138	Nervous system	48.92	48.71	48.74		167	Gallbladder	48.42	48.11	48.18
139	Lung	45.67	45.71	45.72		168	Stomach	47.30	47.40	47.44
140	Non-melanoma BCC	46.46	46.20	46.32		169	Pancreas	46.06	46.27	46.29
141	Lung	47.21	47.02	47.06		170	Lung	49.61	49.77	49.78
142	Lung	47.63	47.89	47.90		171	Stomach	48.74	48.60	48.64
143	Lung	48.24	48.36	48.38		172	Non-melanoma SCC	46.88	46.60	46.61
144	Gallbladder	45.70	45.67	45.76		173	Lymphoma and multiple myeloma	47.23	47.36	47.39
145	Non-melanoma BCC	46.48	46.52	46.82		174	All Male Genitalia	49.05	49.04	49.06
146	Non-melanoma SCC	47.14	47.24	47.25		175	Non-melanoma BCC	49.81	49.90	49.92
147	Lung	47.69	47.50	47.51						
148	Lung	48.25	48.39	48.40						
149	Lung	48.87	48.90	48.94						

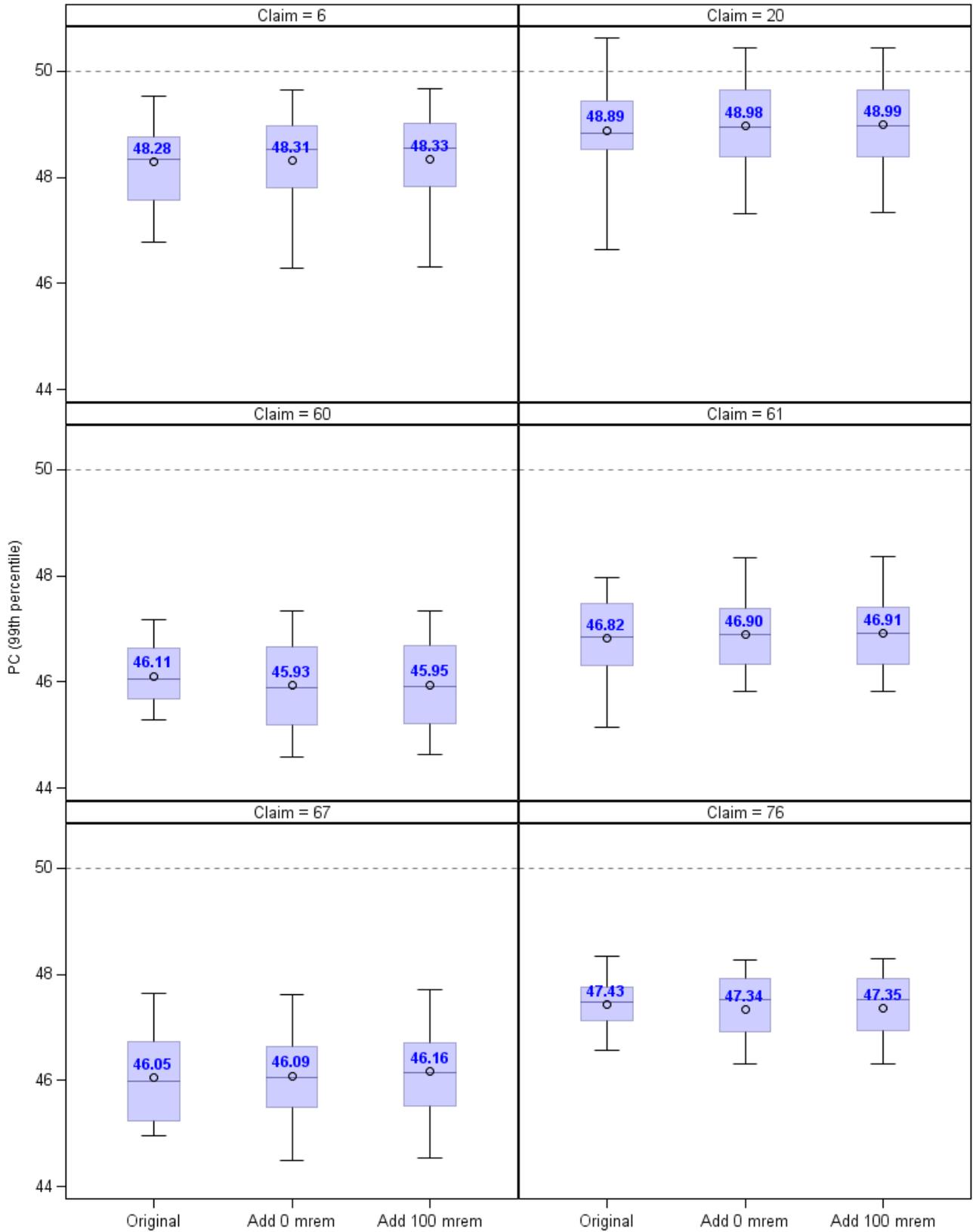
## **Attachment 2**

This attachment provides side-by-side box plots for the 99<sup>th</sup> percentile PC values from the three dose scenarios for each of the 175 cases. The cases are grouped by IREP cancer model.

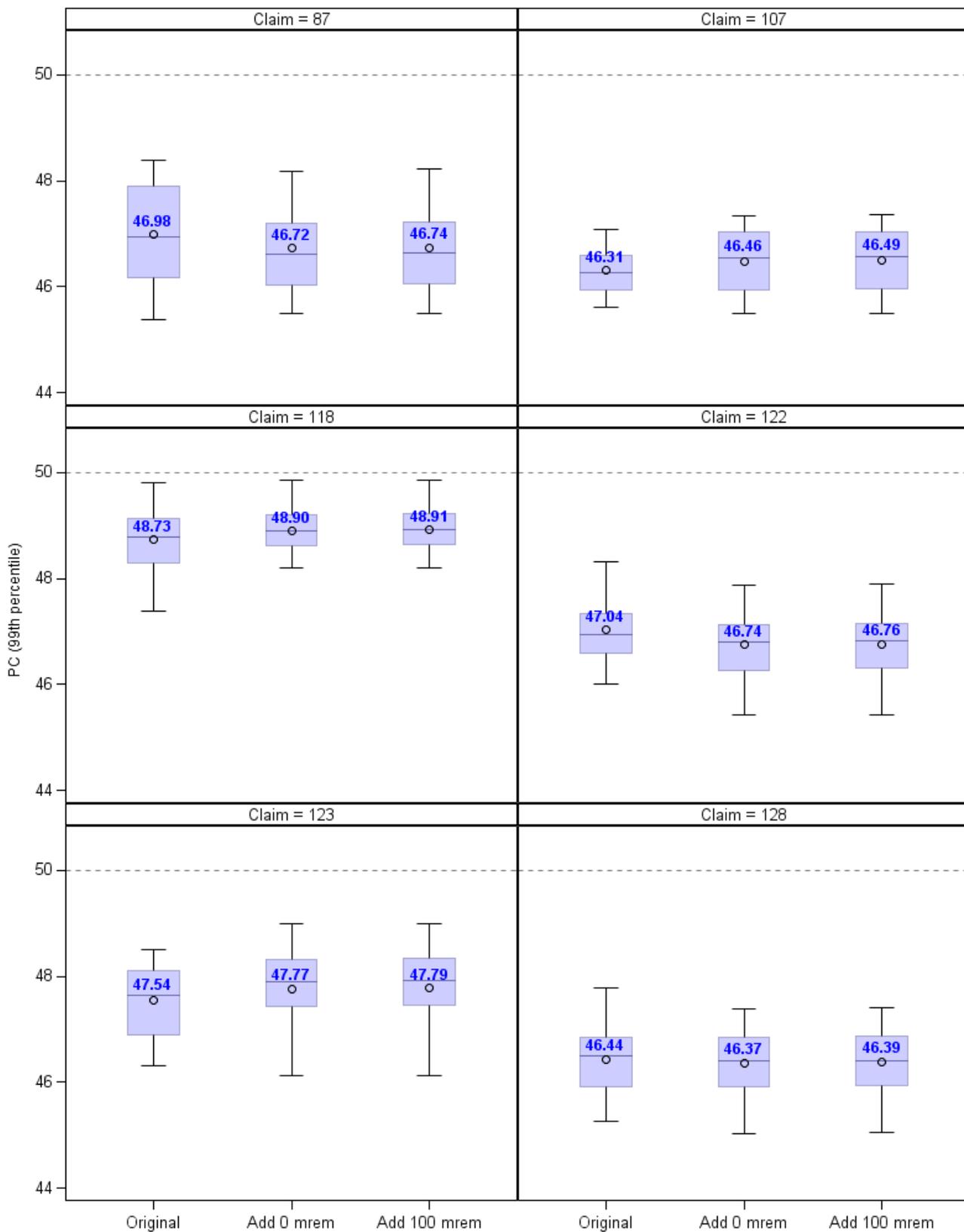
### IREP Cancer Model = Acute Myeloid Leukemia



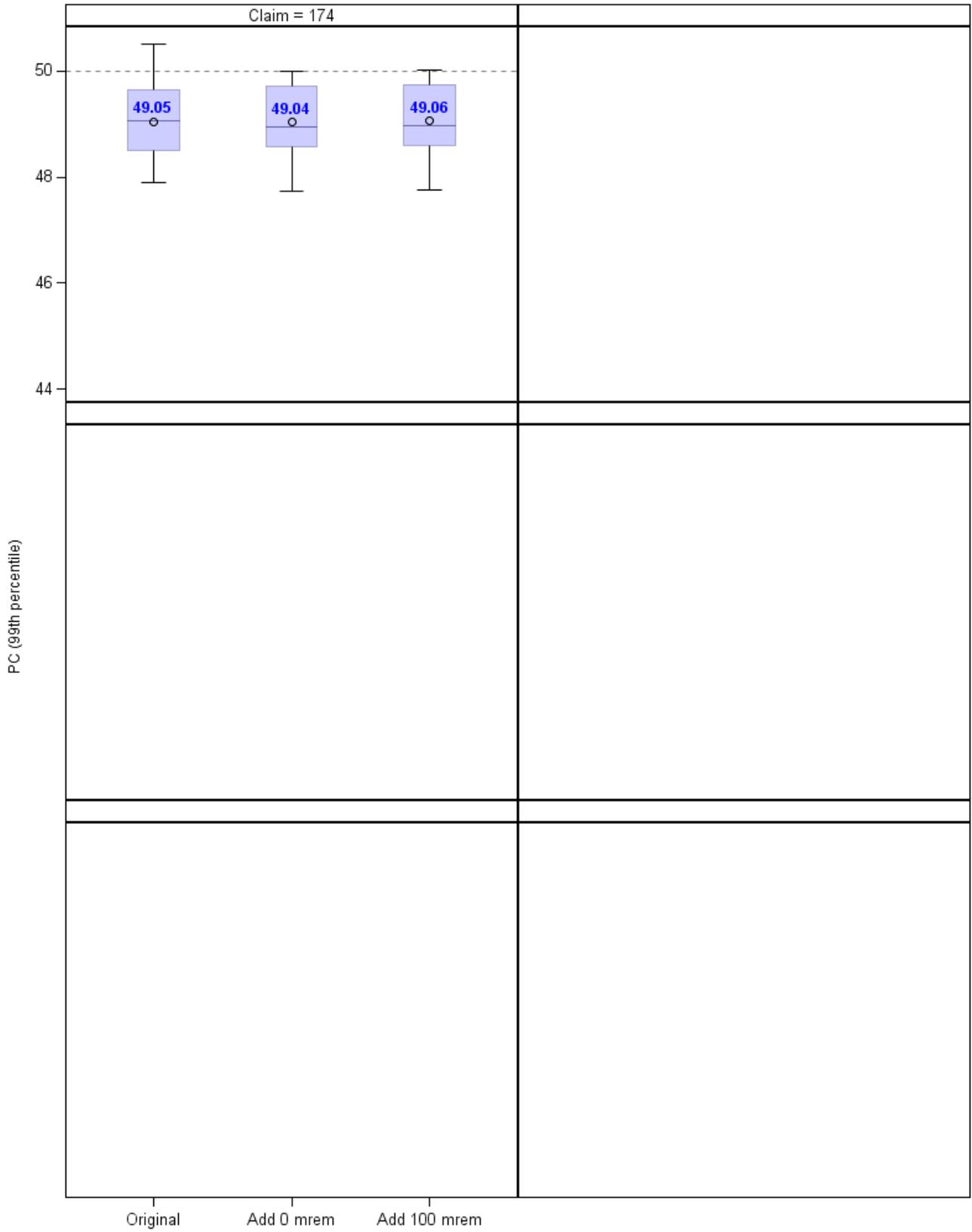
IREP Cancer Model = All Male Genitalia



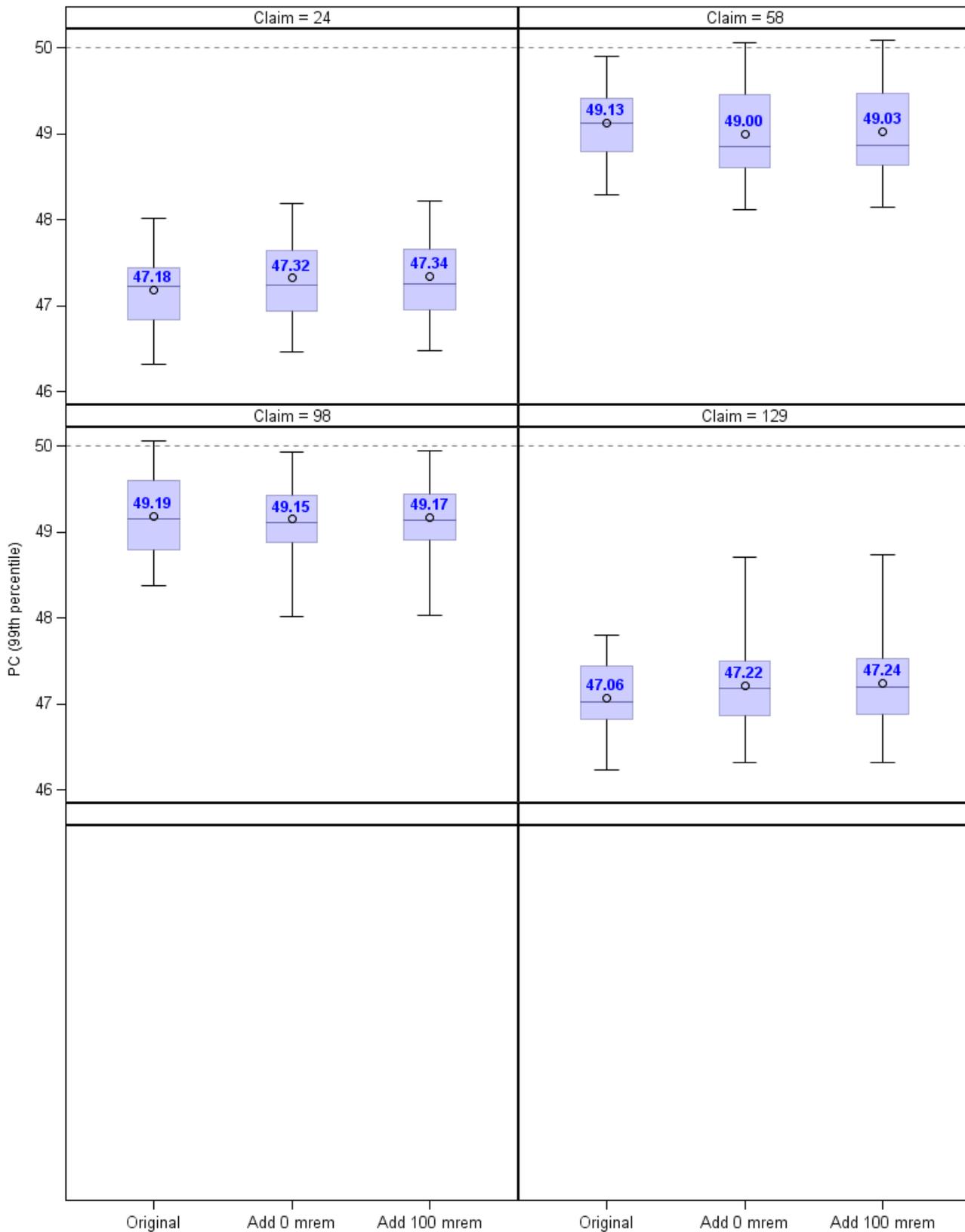
IREP Cancer Model = All Male Genitalia



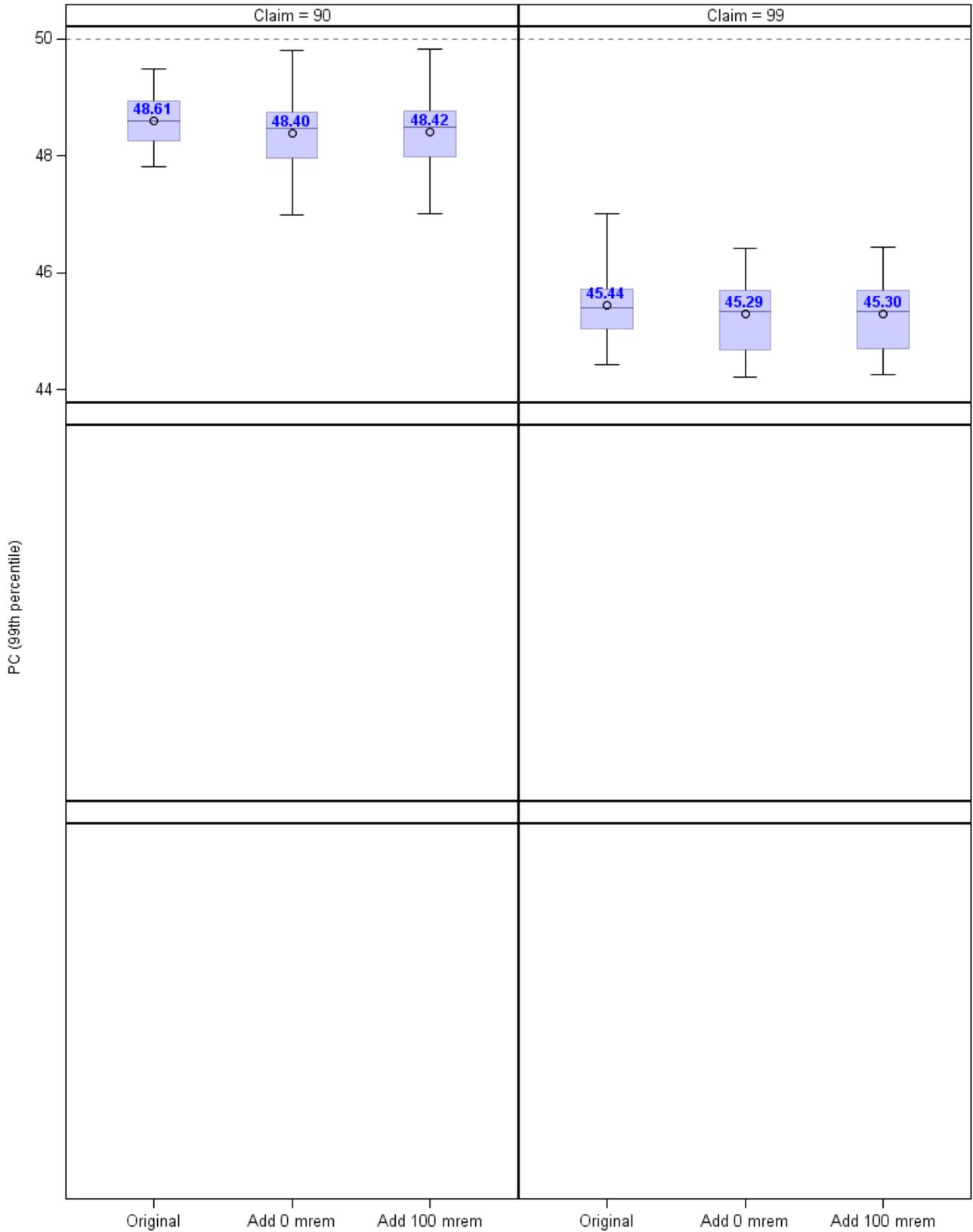
IREP Cancer Model = All Male Genitalia



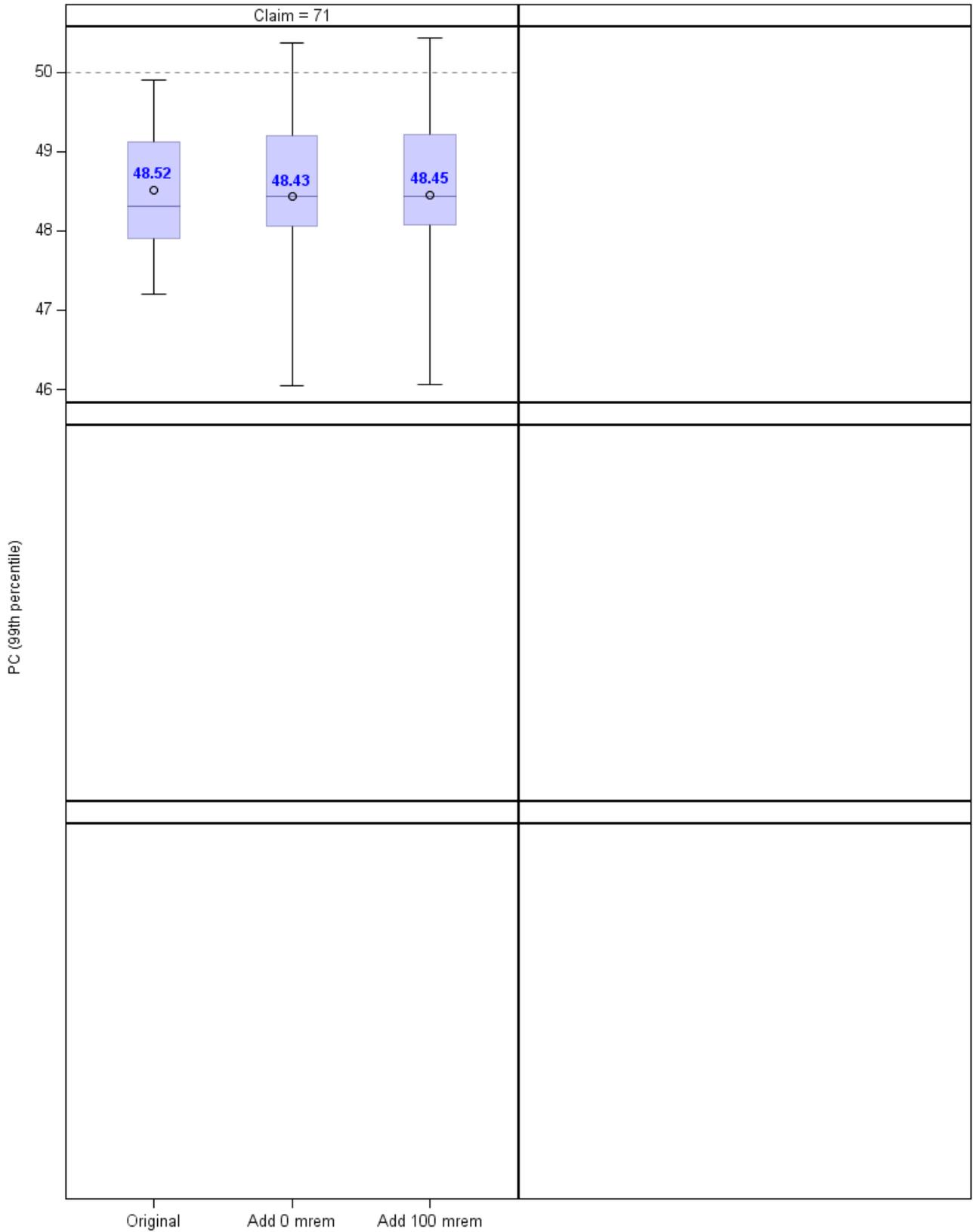
IREP Cancer Model = Bladder



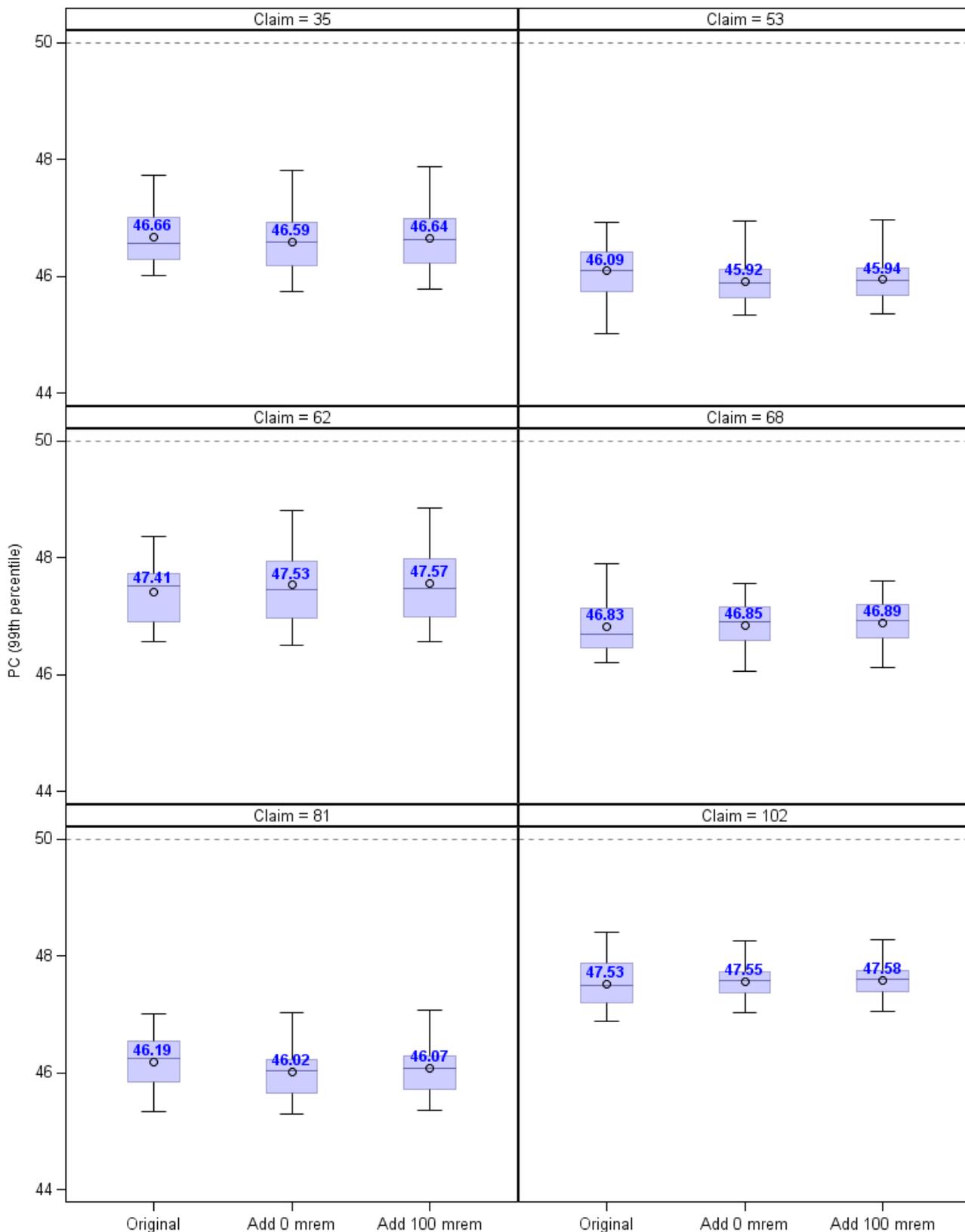
IREP Cancer Model = Bone



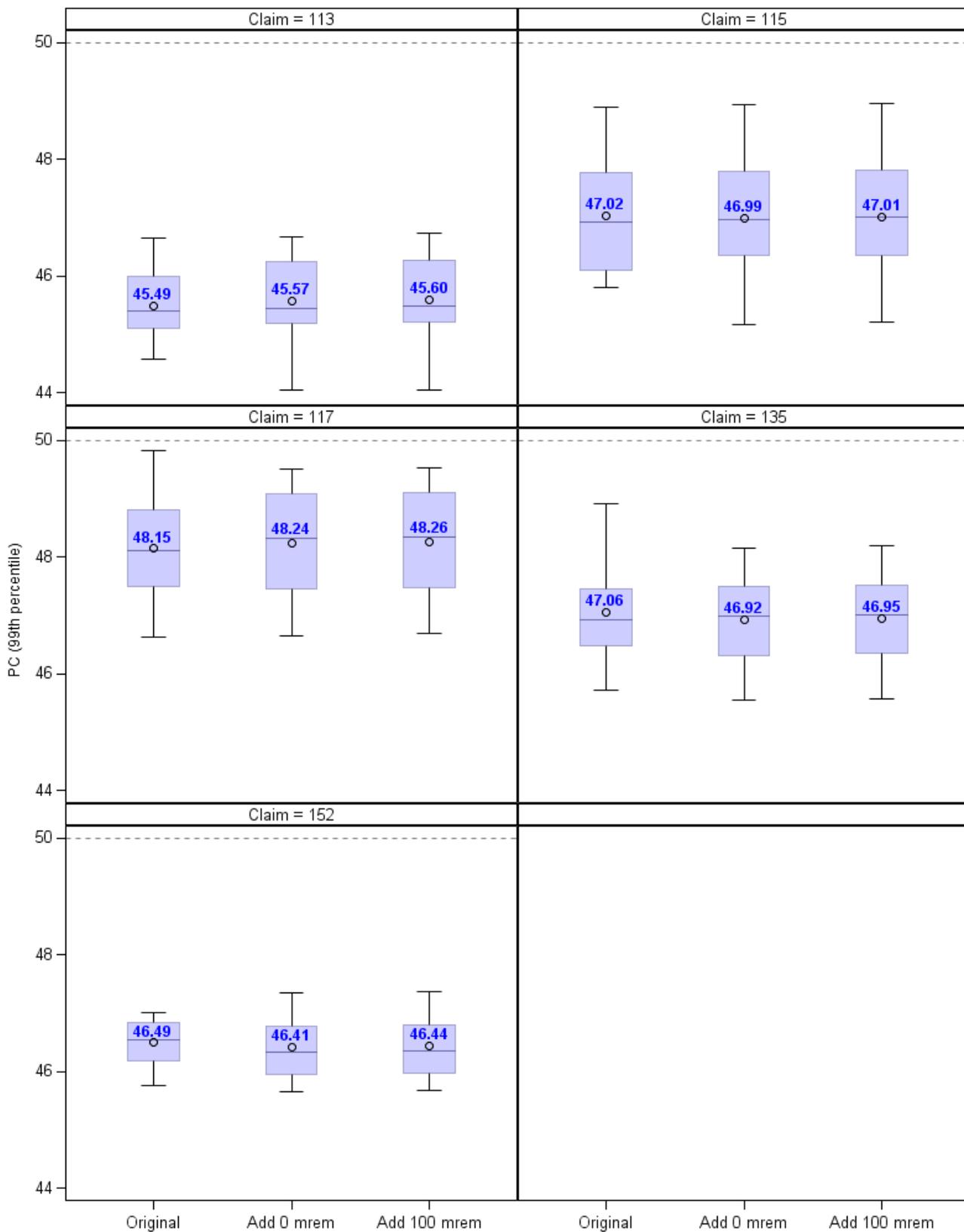
### IREP Cancer Model = Chronic Lymphocytic Leukemia



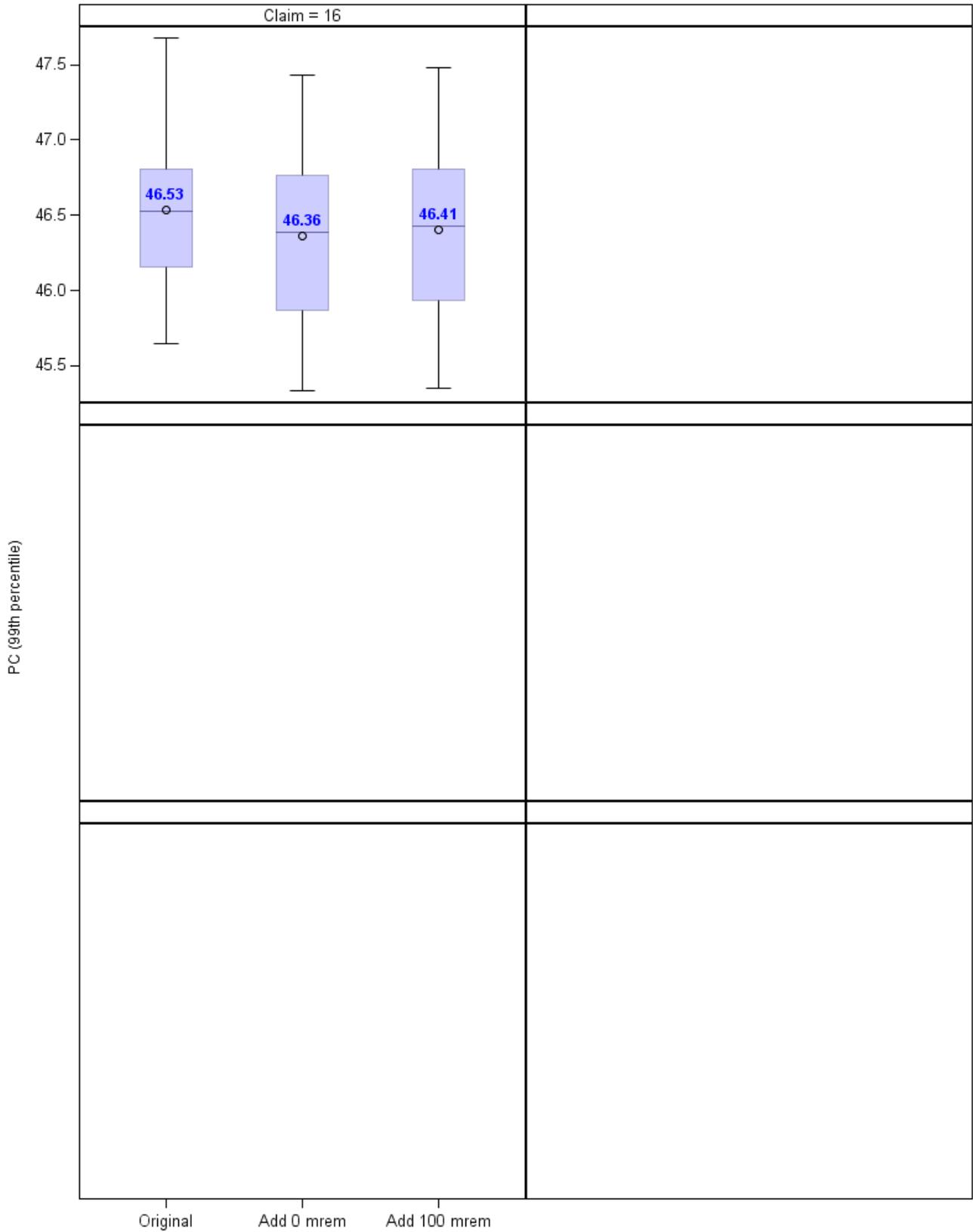
IREP Cancer Model = Colon



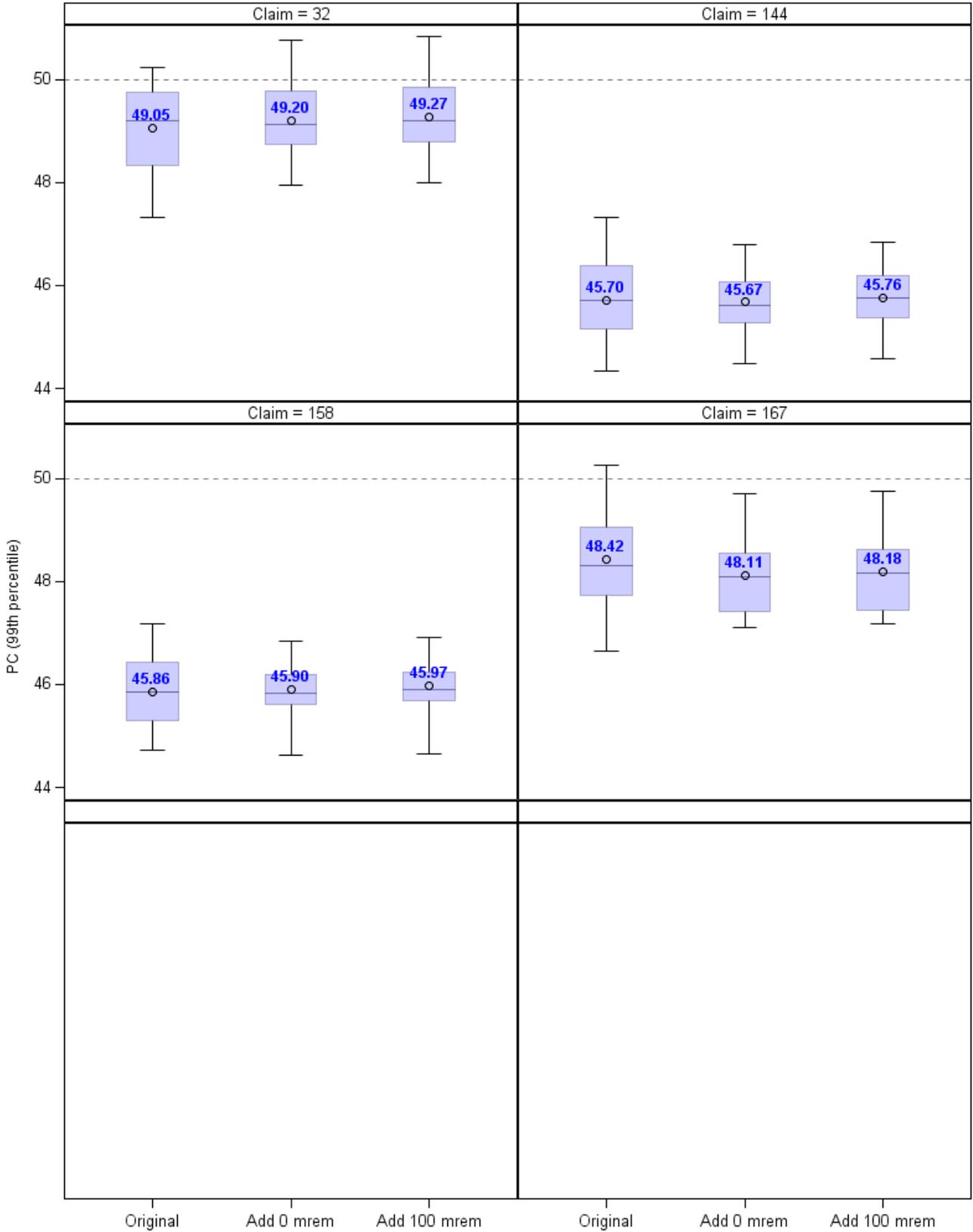
IREP Cancer Model = Colon



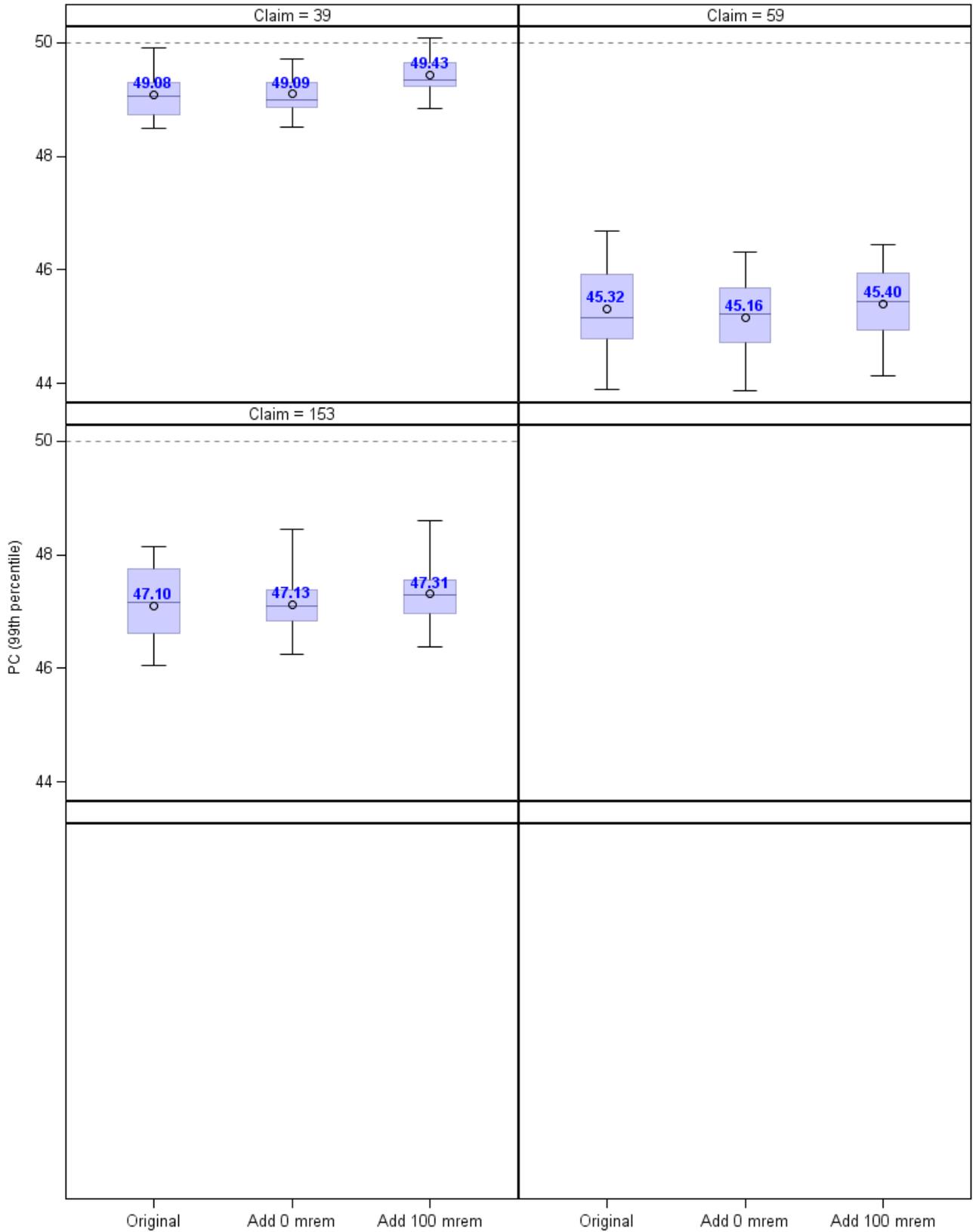
IREP Cancer Model = Connective tissue



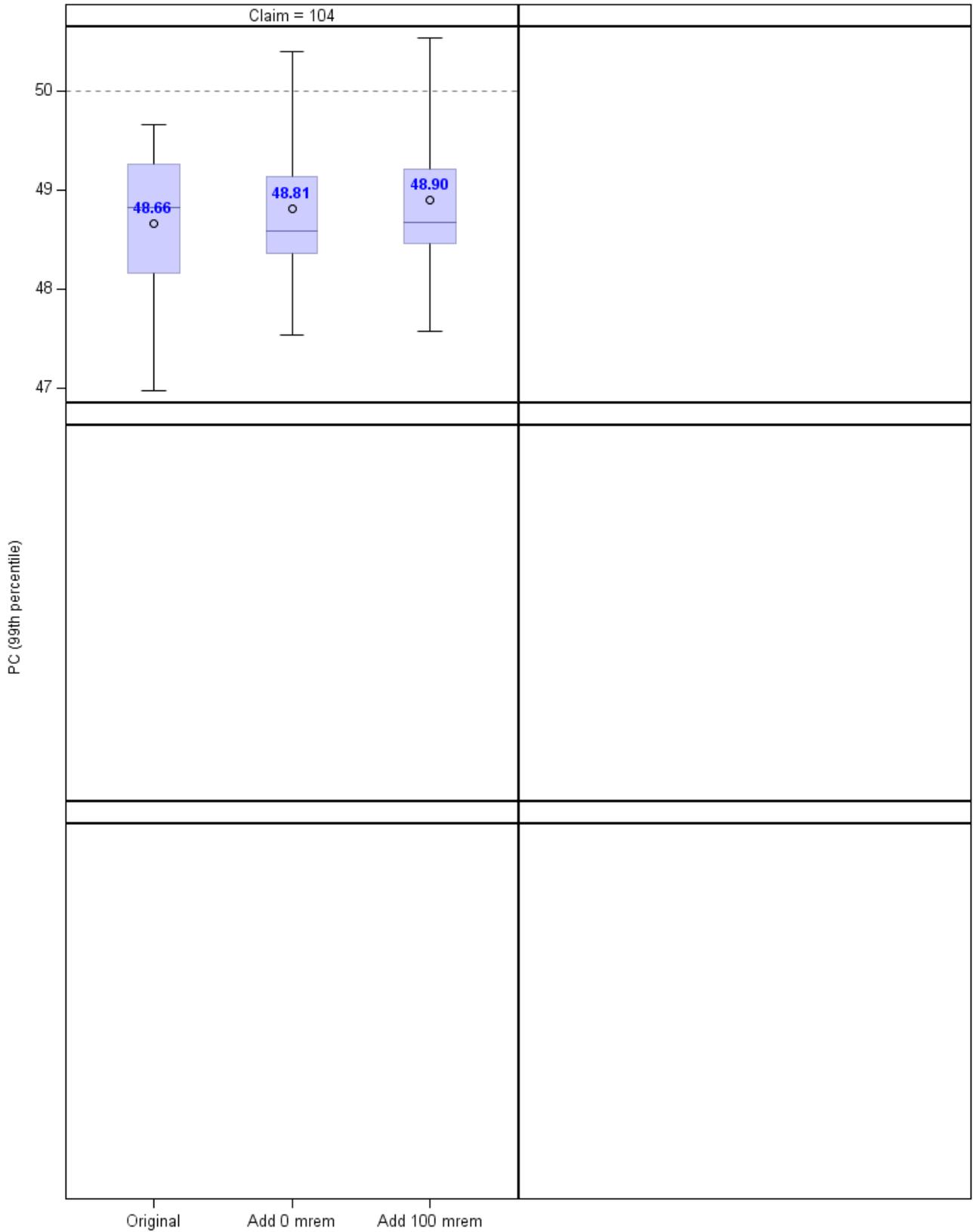
IREP Cancer Model = Gallbladder



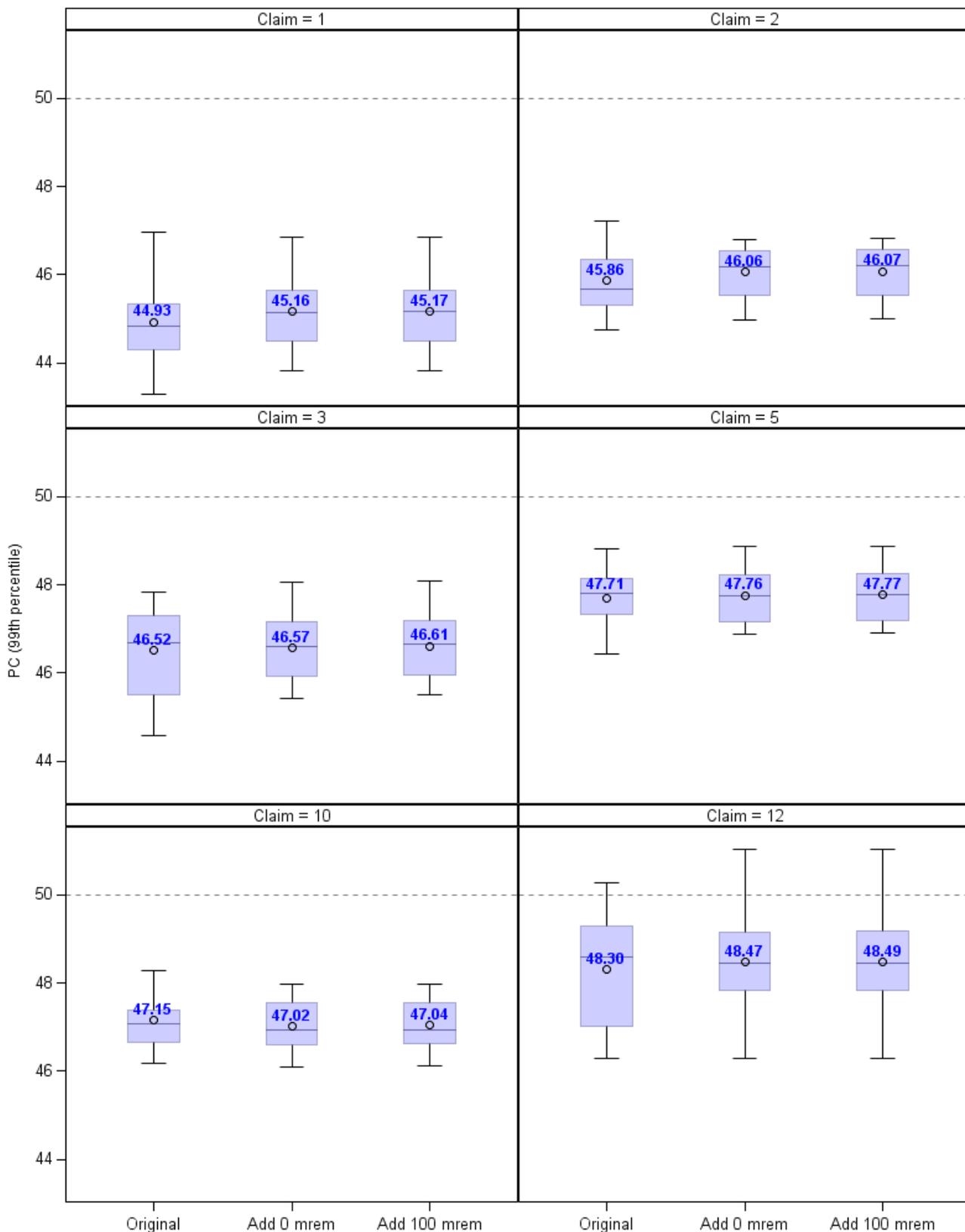
IREP Cancer Model = Leukemia (excl. CLL)



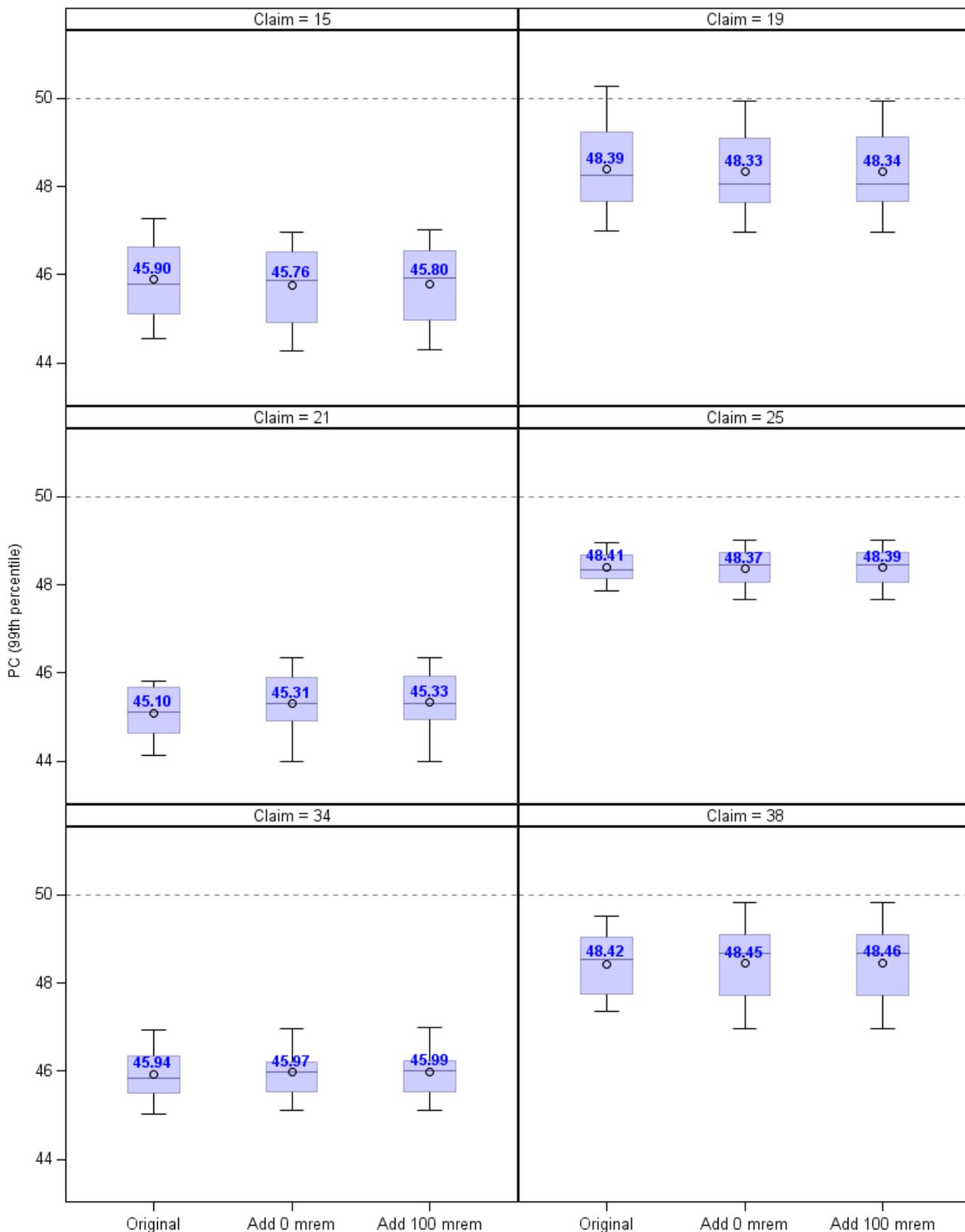
IREP Cancer Model = Liver



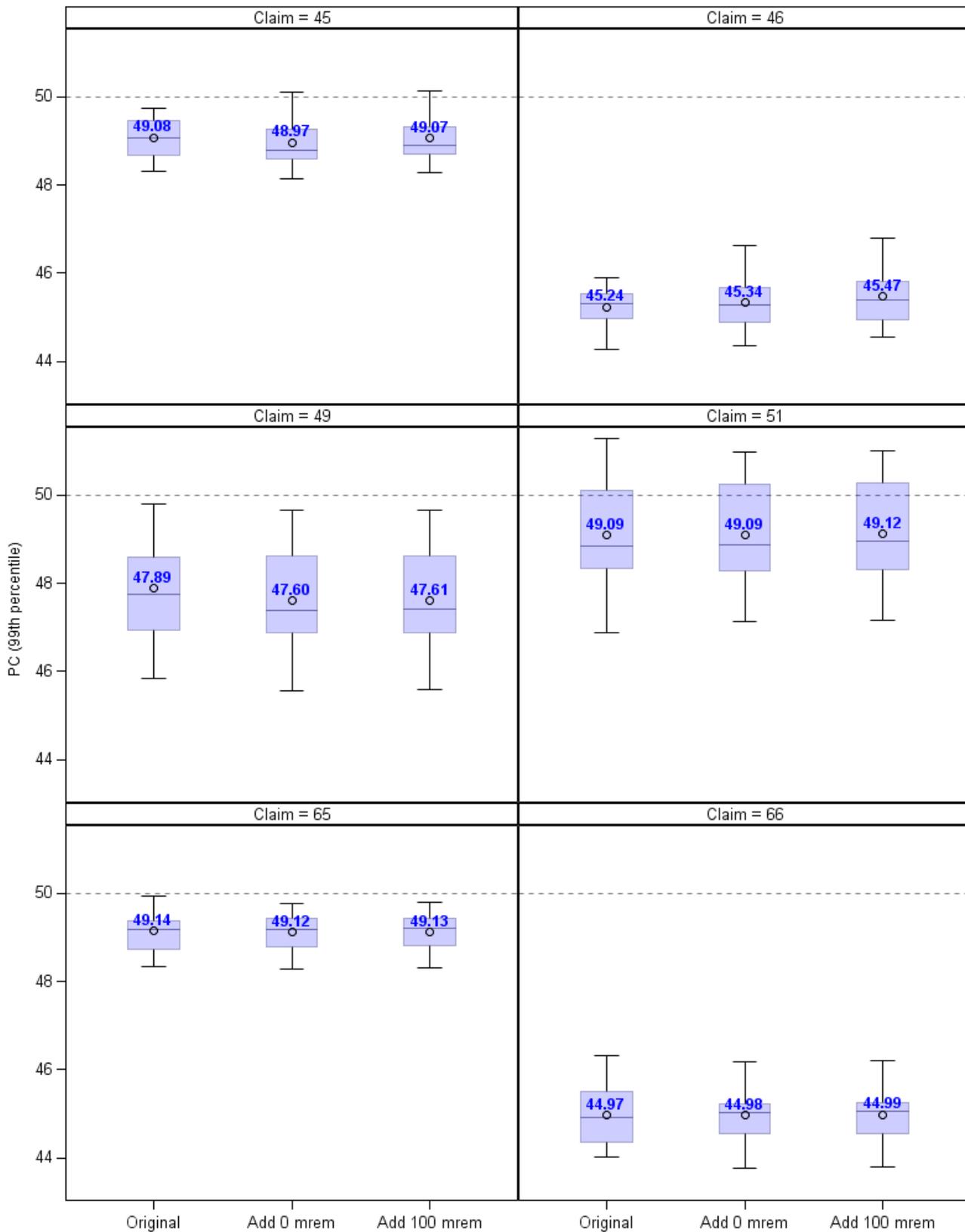
IREP Cancer Model = Lung



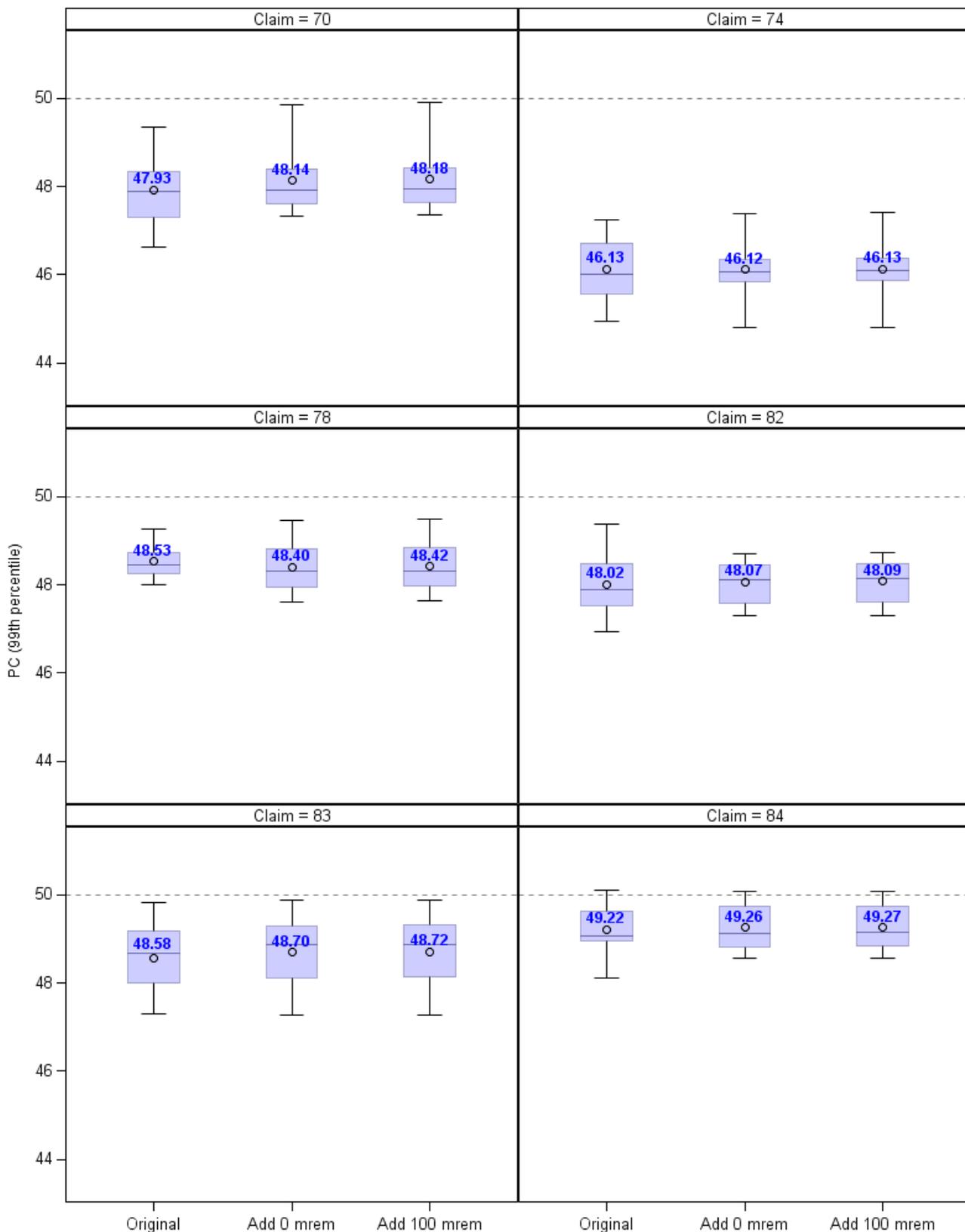
IREP Cancer Model = Lung



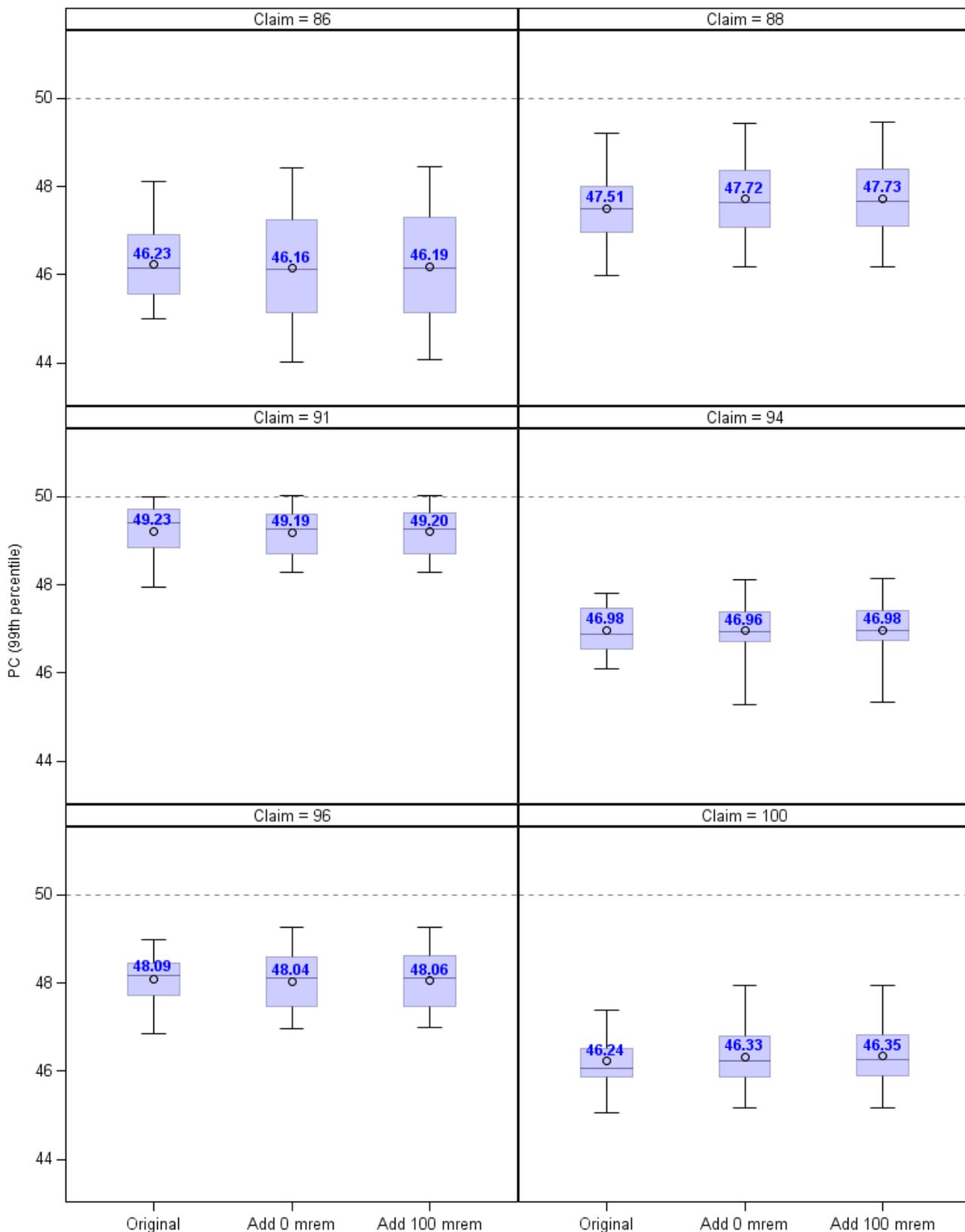
IREP Cancer Model = Lung



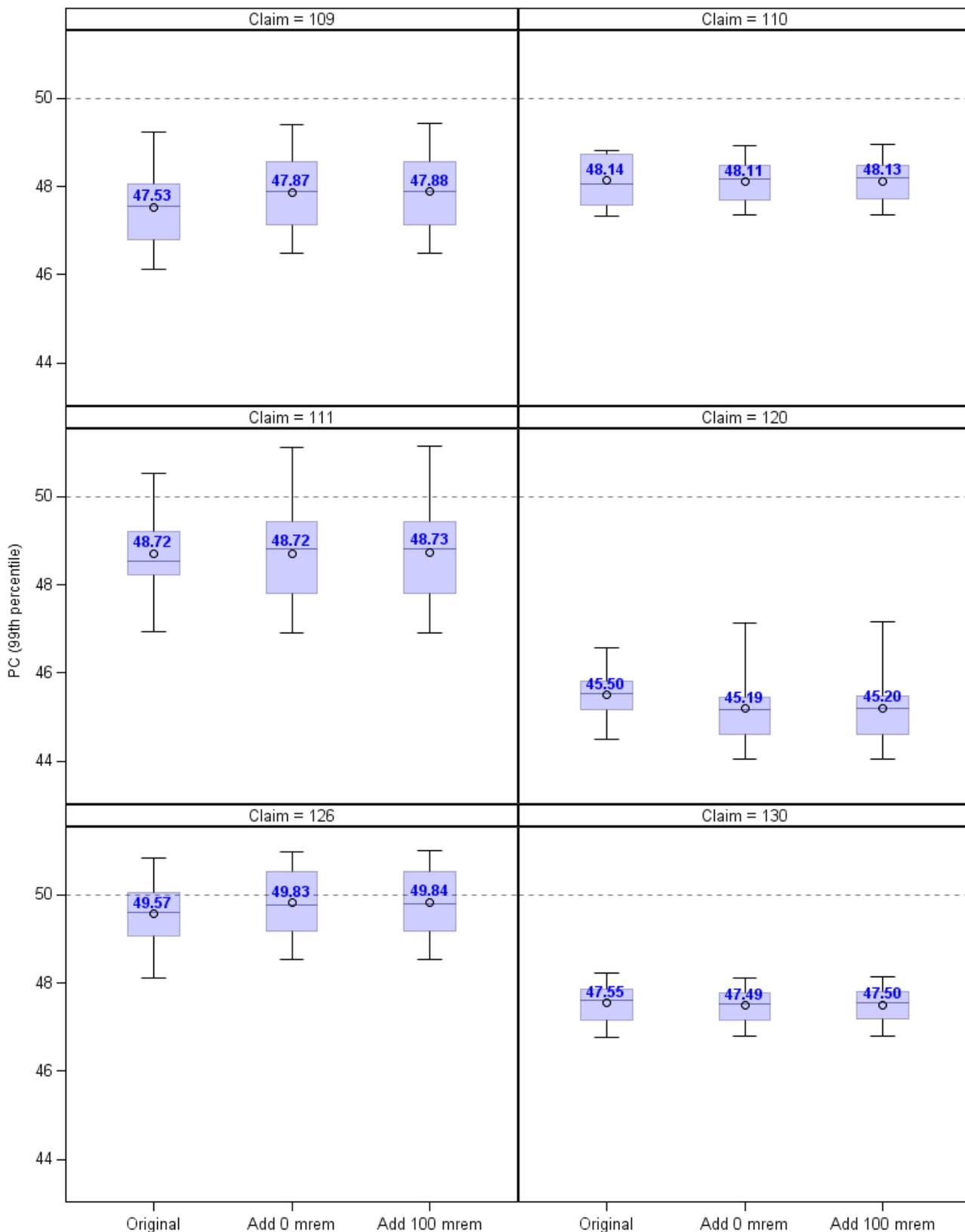
IREP Cancer Model = Lung



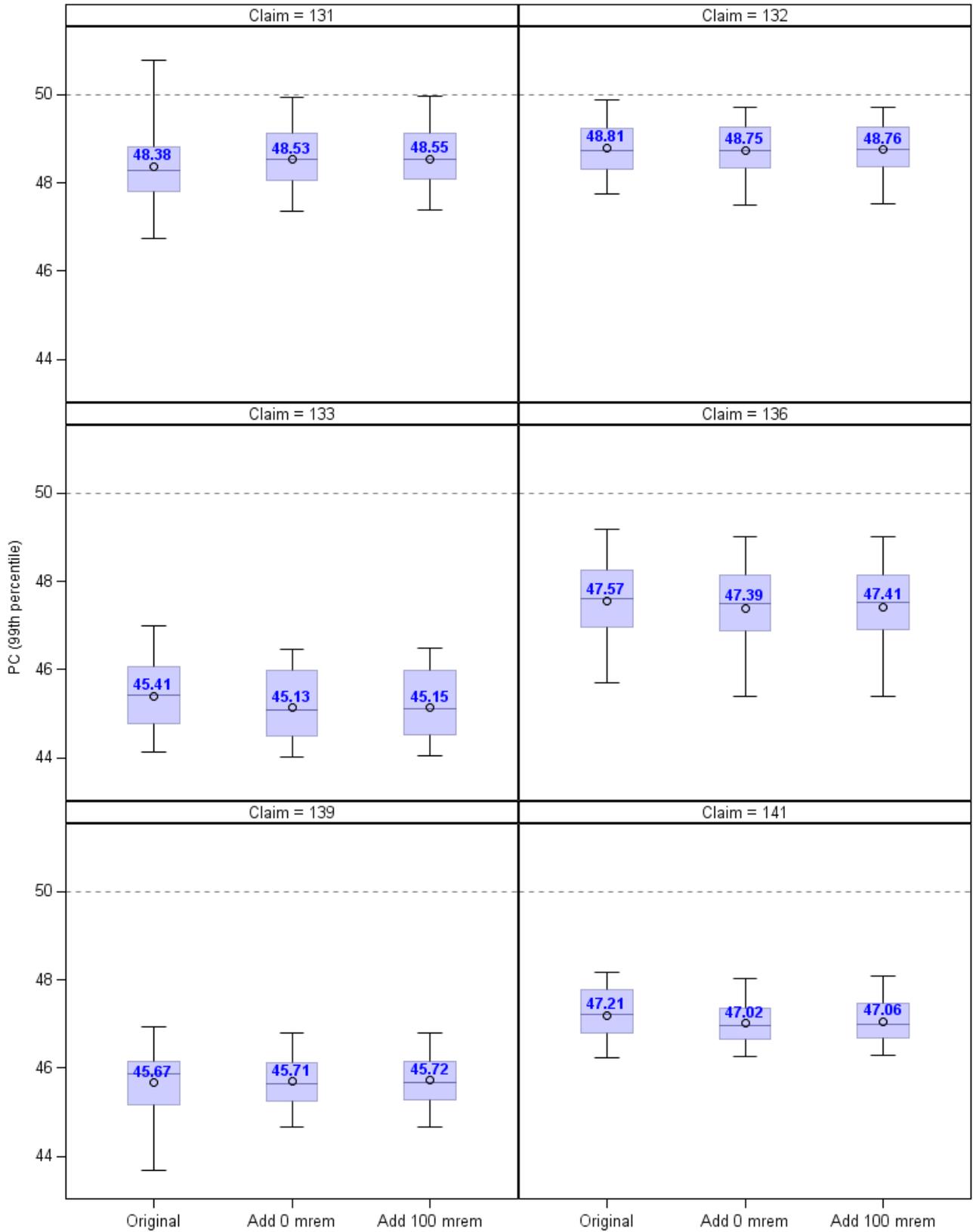
IREP Cancer Model = Lung



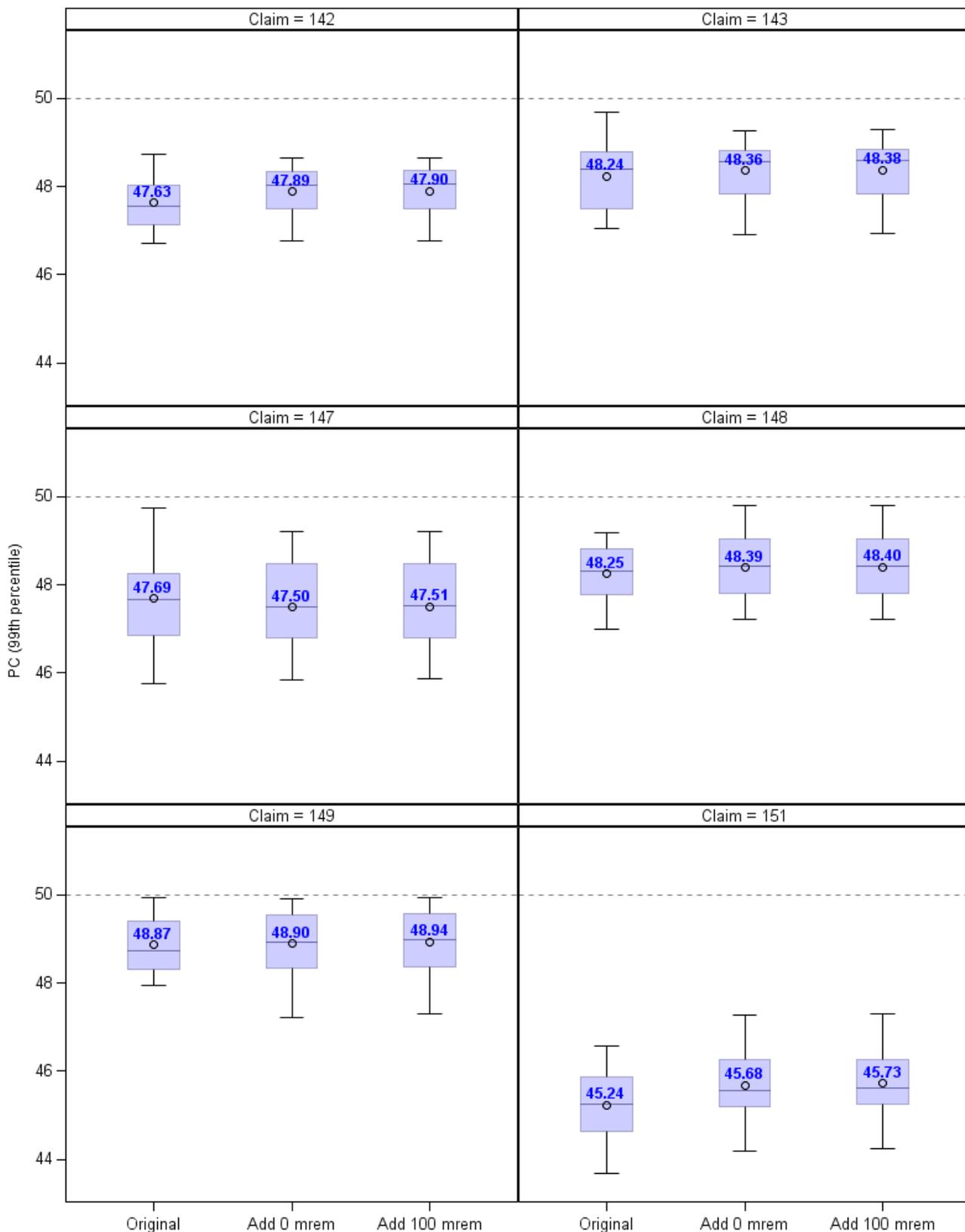
IREP Cancer Model = Lung



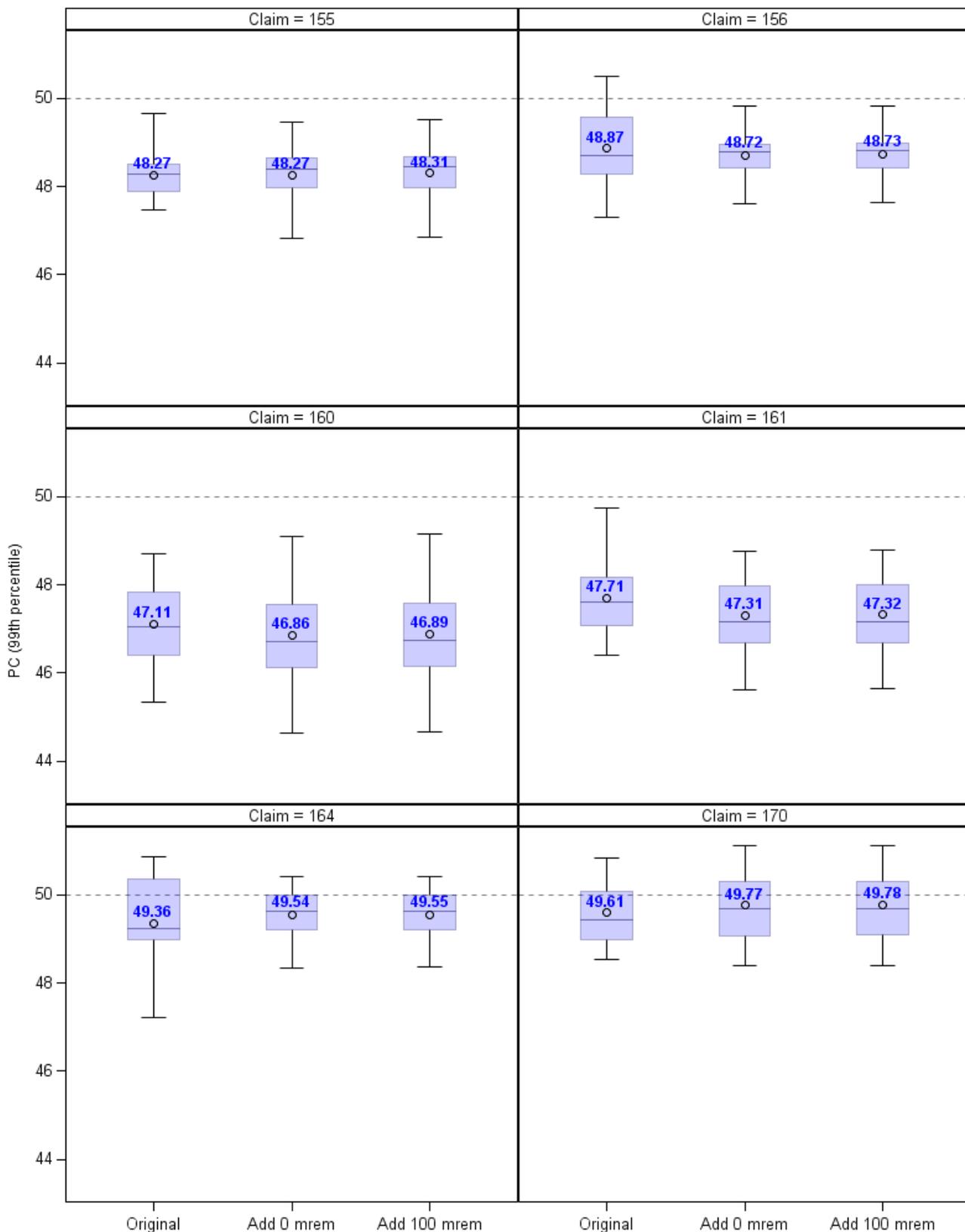
IREP Cancer Model = Lung



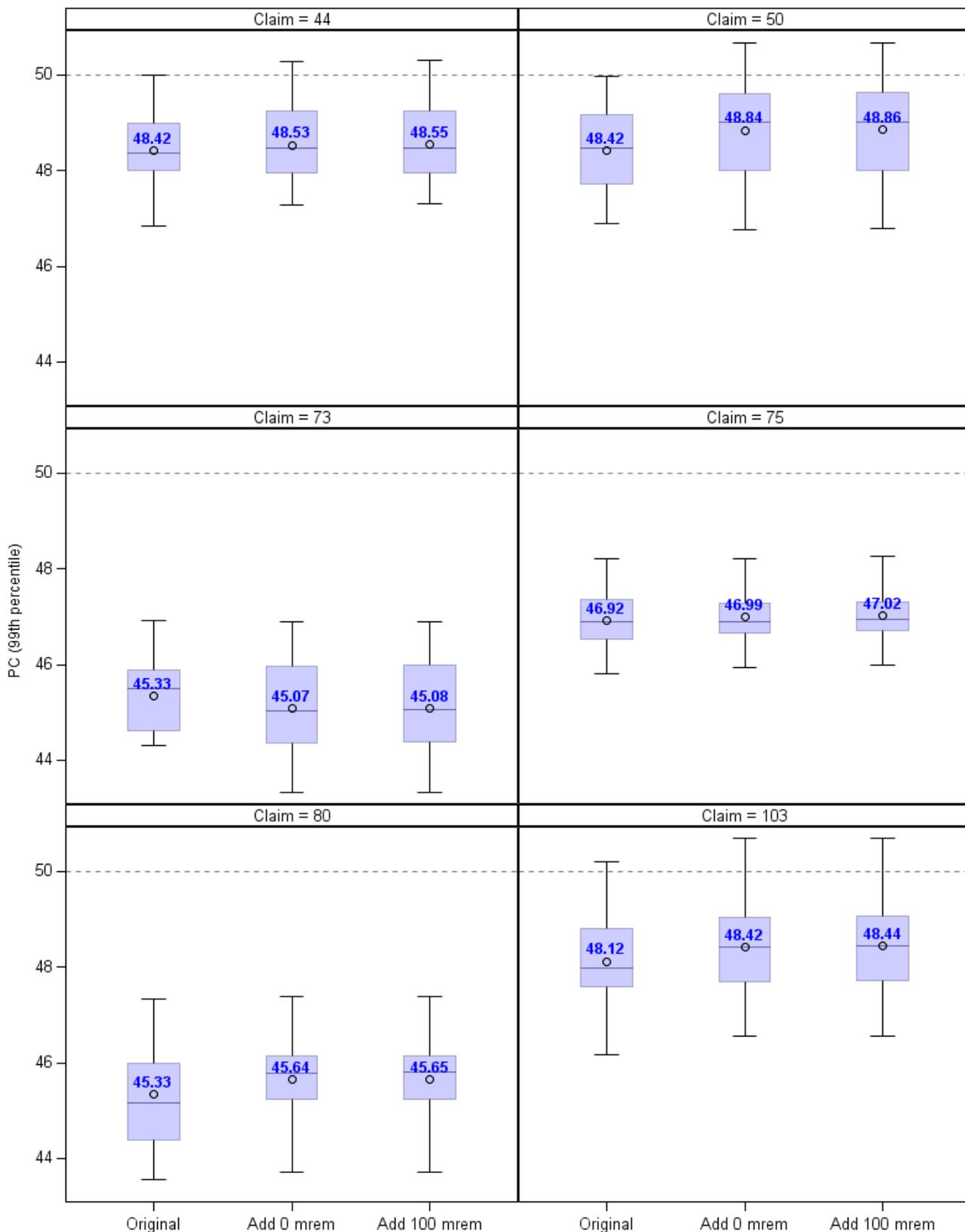
IREP Cancer Model = Lung



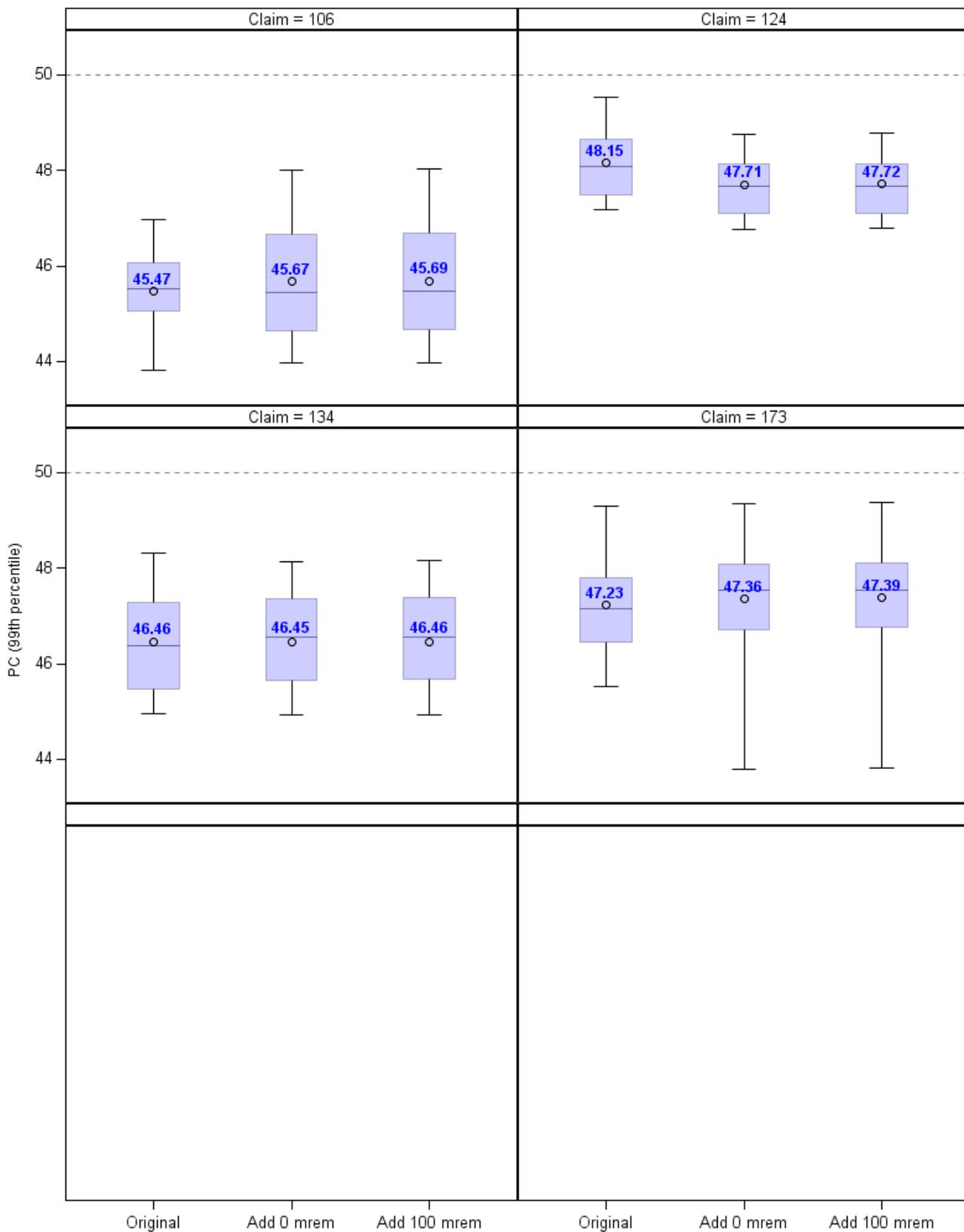
IREP Cancer Model = Lung



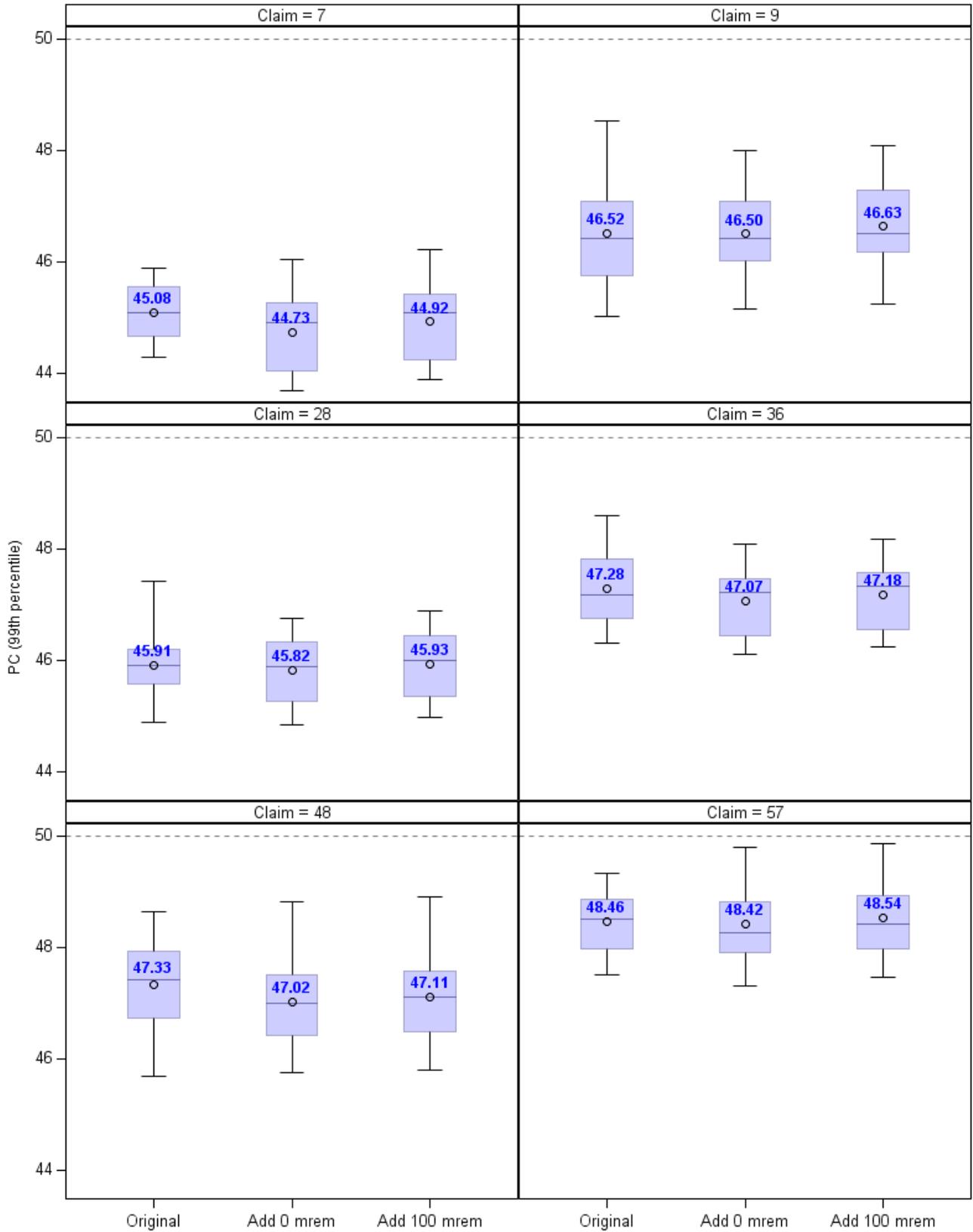
IREP Cancer Model = Lymphoma and multiple myeloma



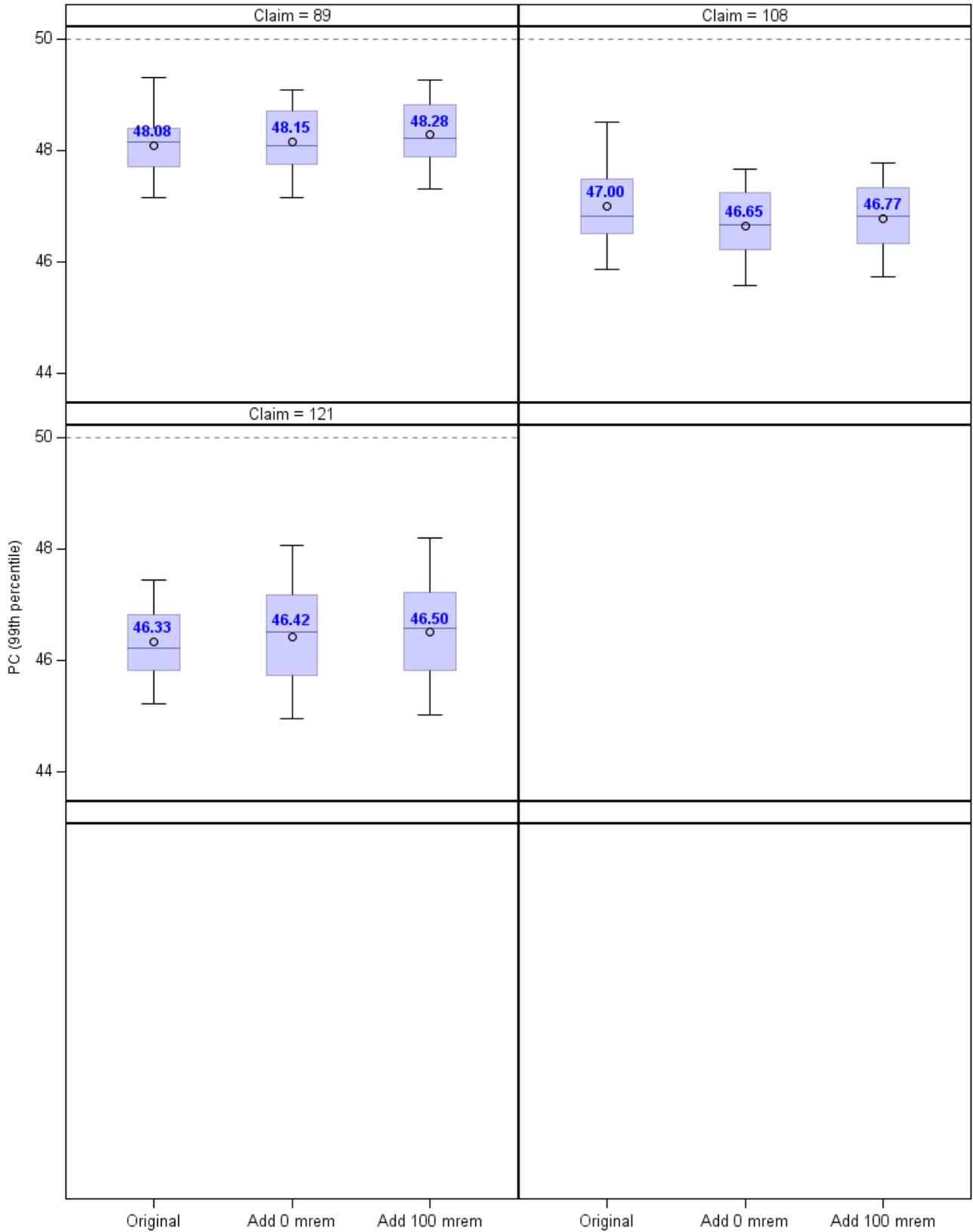
IREP Cancer Model = Lymphoma and multiple myeloma



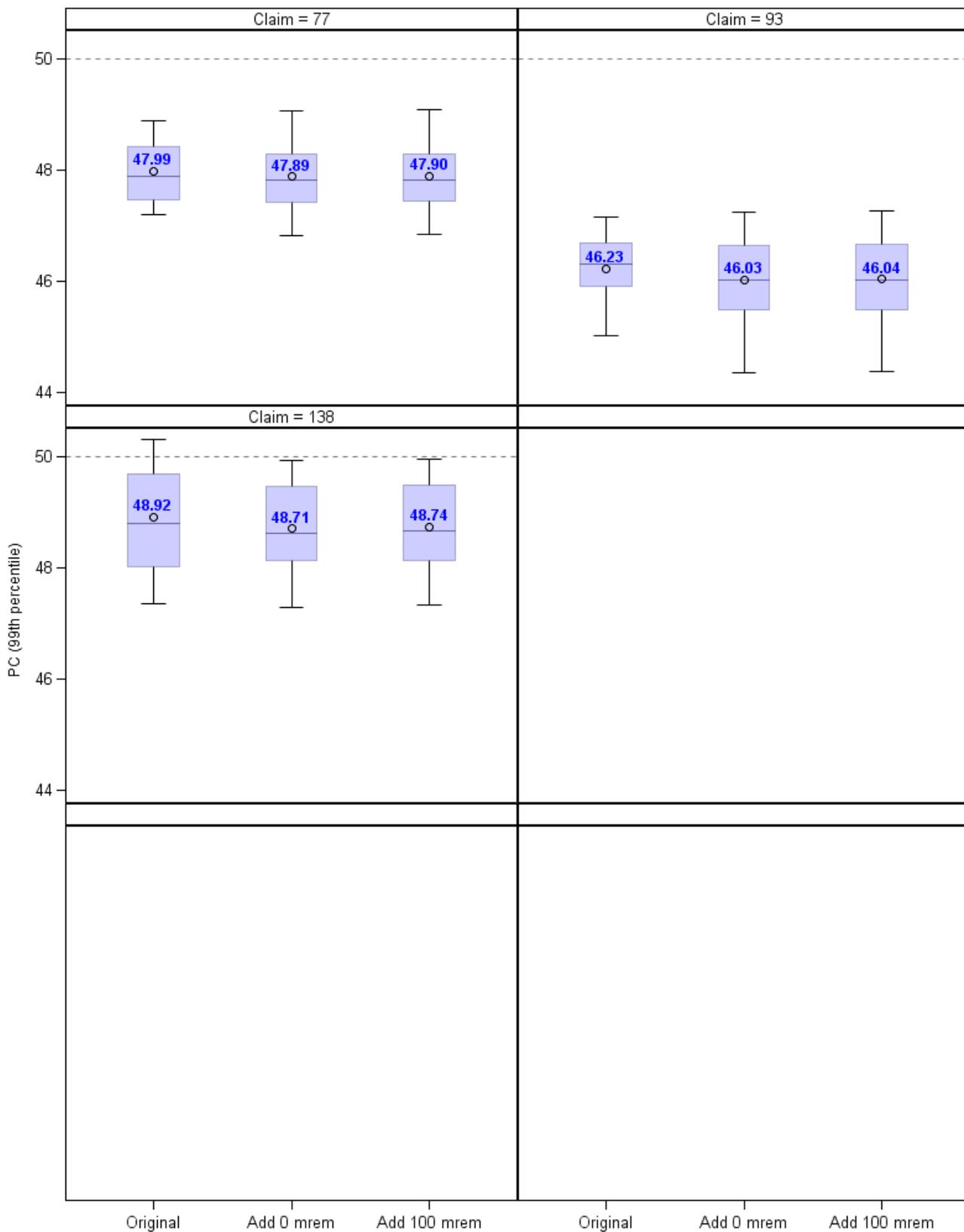
IREP Cancer Model = Malignant melanoma



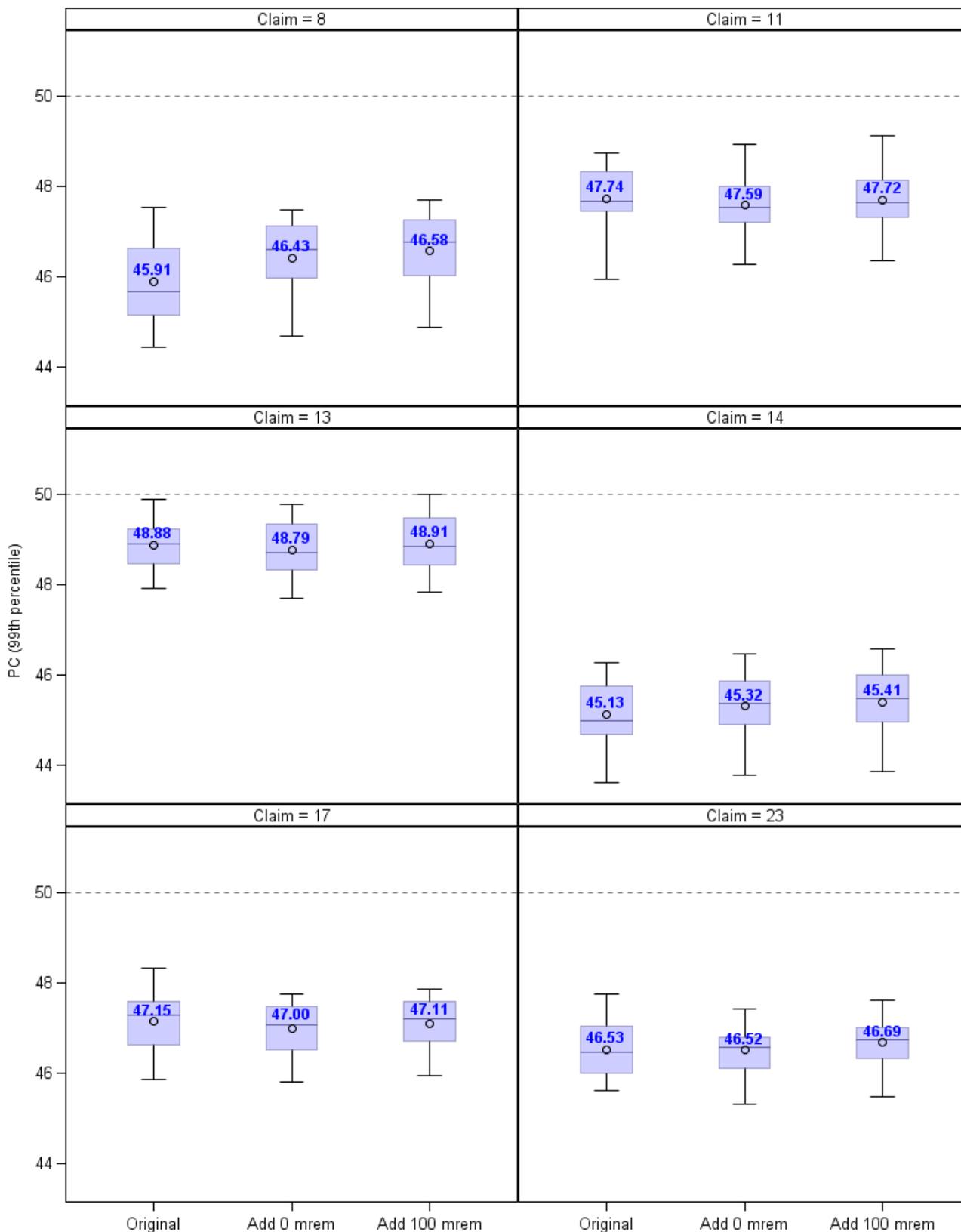
IREP Cancer Model = Malignant melanoma



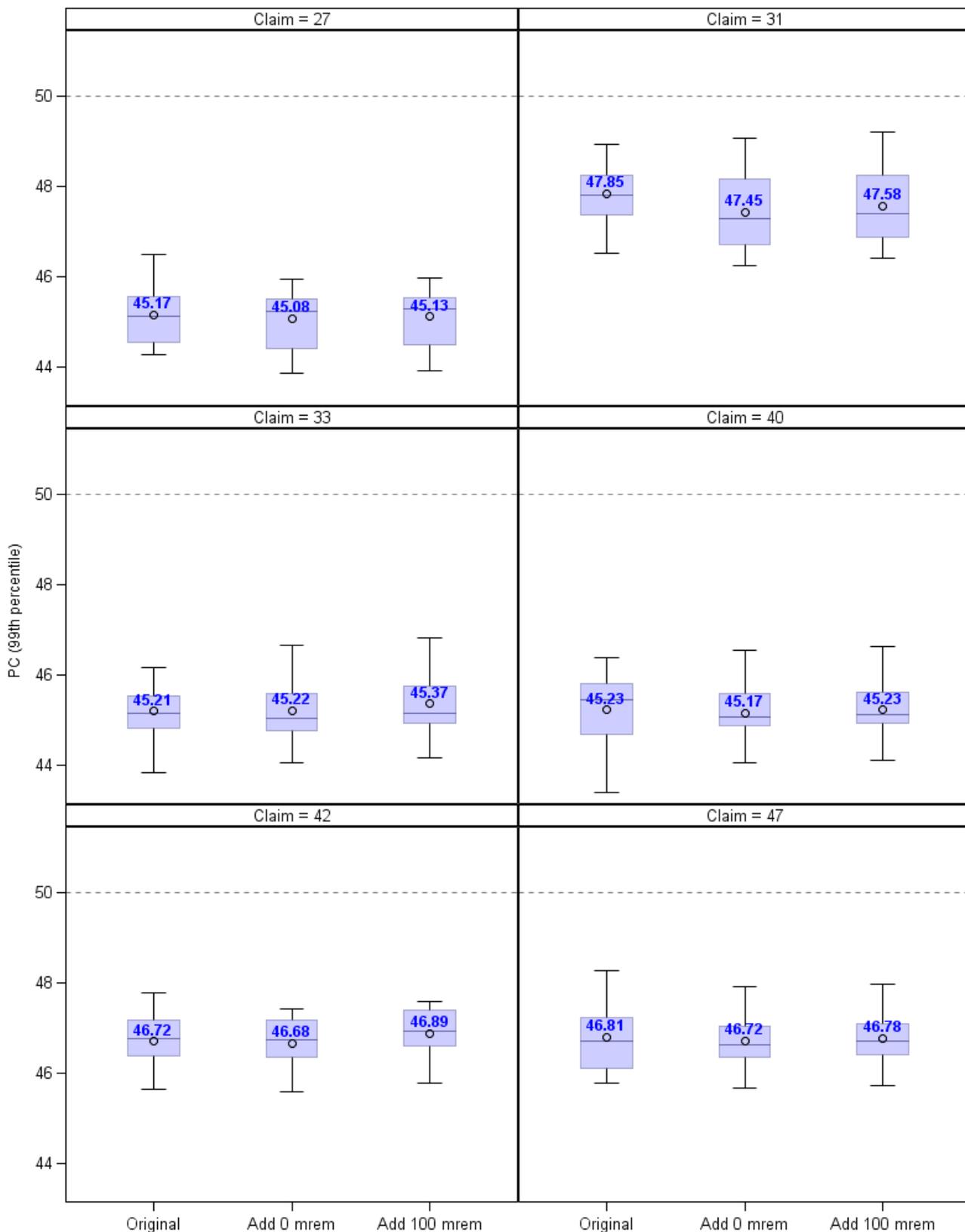
IREP Cancer Model = Nervous system



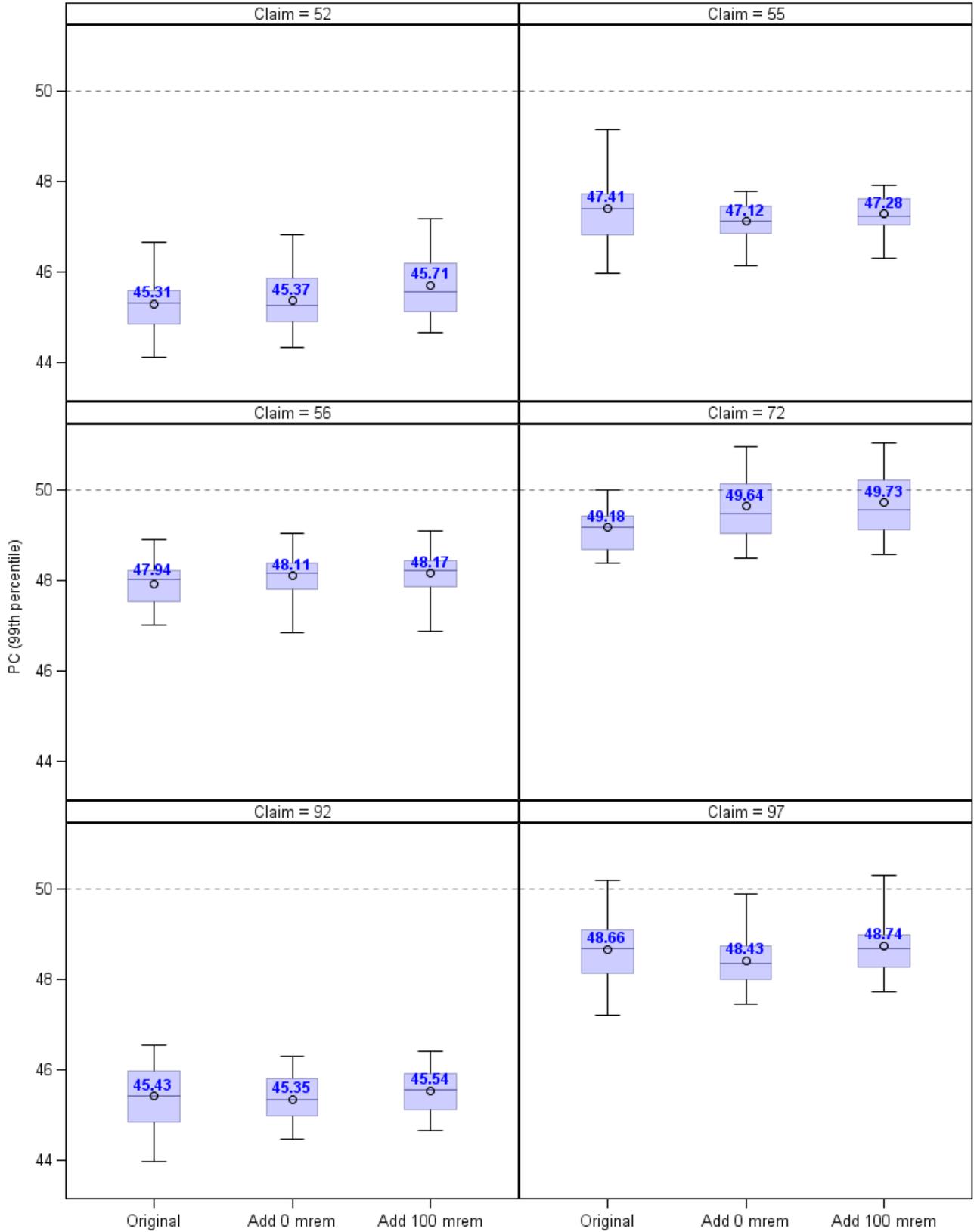
IREP Cancer Model = Non-melanoma BCC



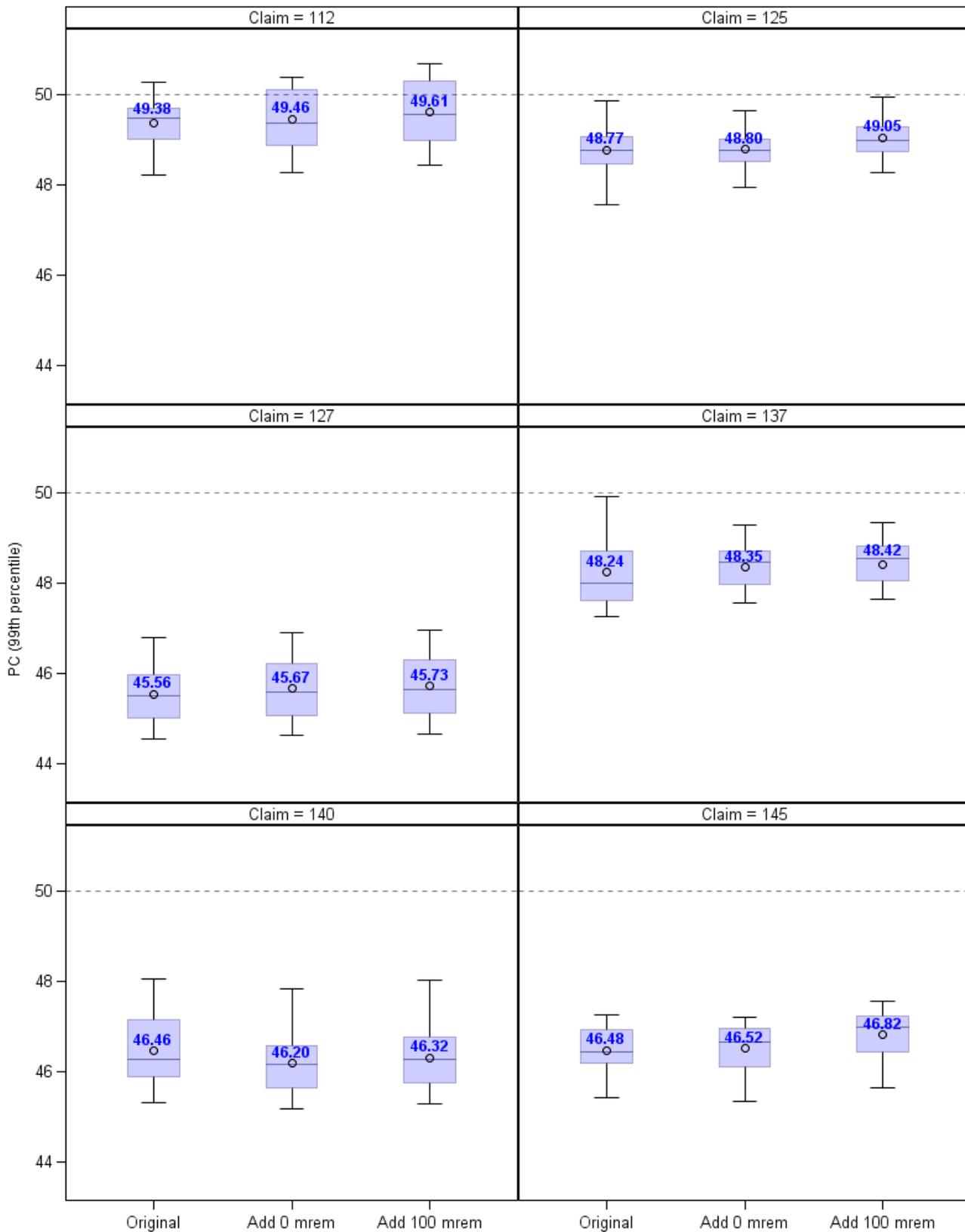
IREP Cancer Model = Non-melanoma BCC



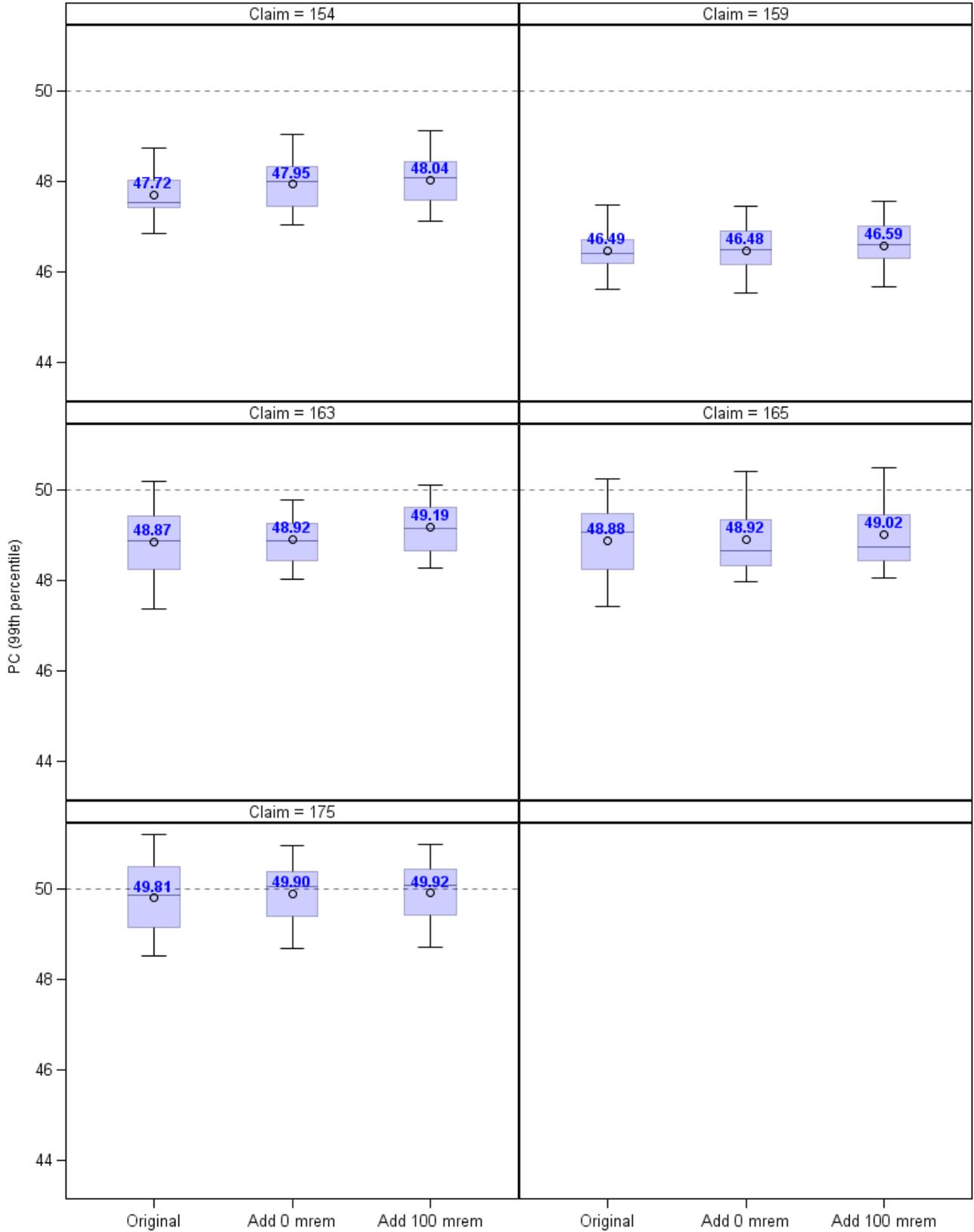
IREP Cancer Model = Non-melanoma BCC



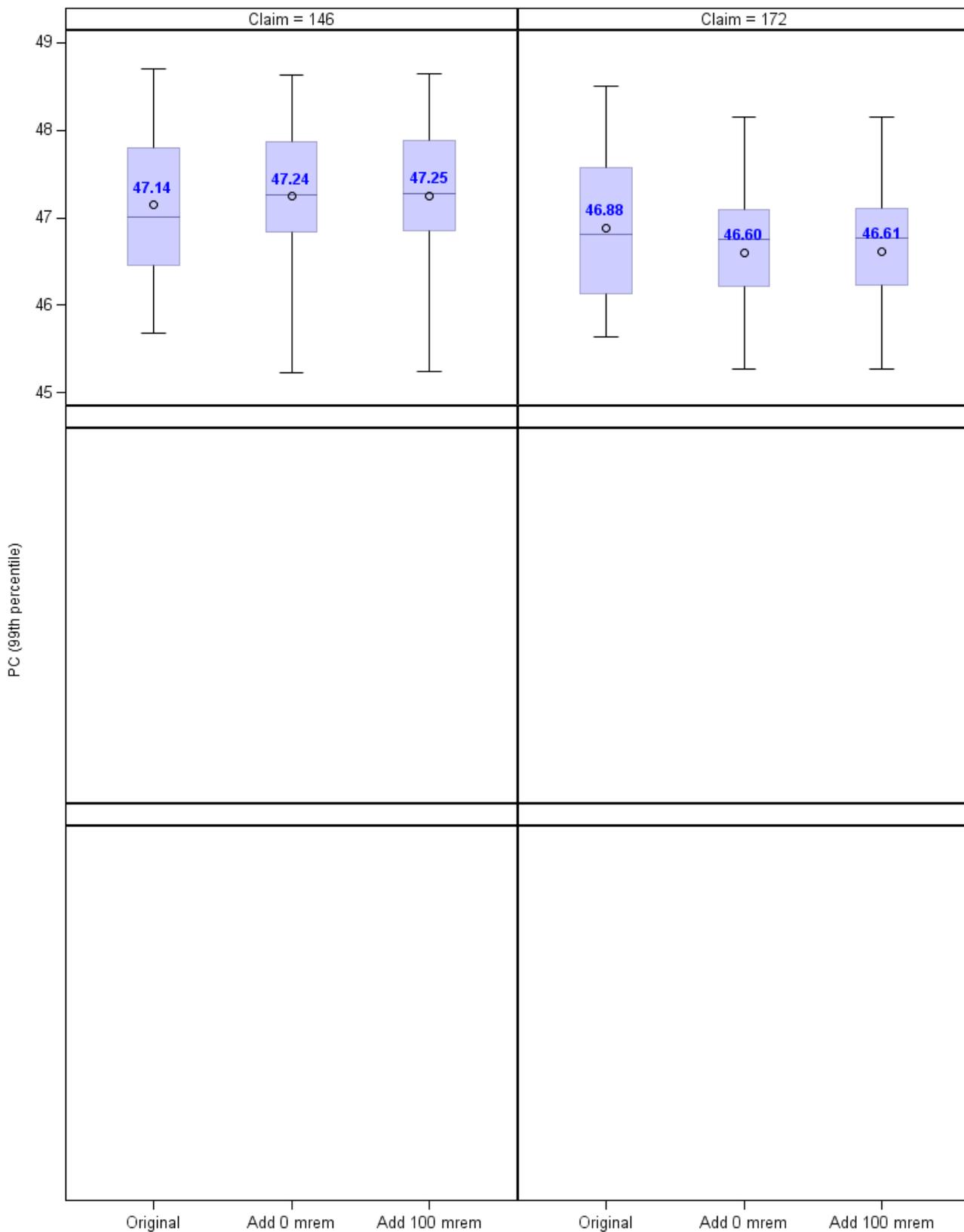
IREP Cancer Model = Non-melanoma BCC



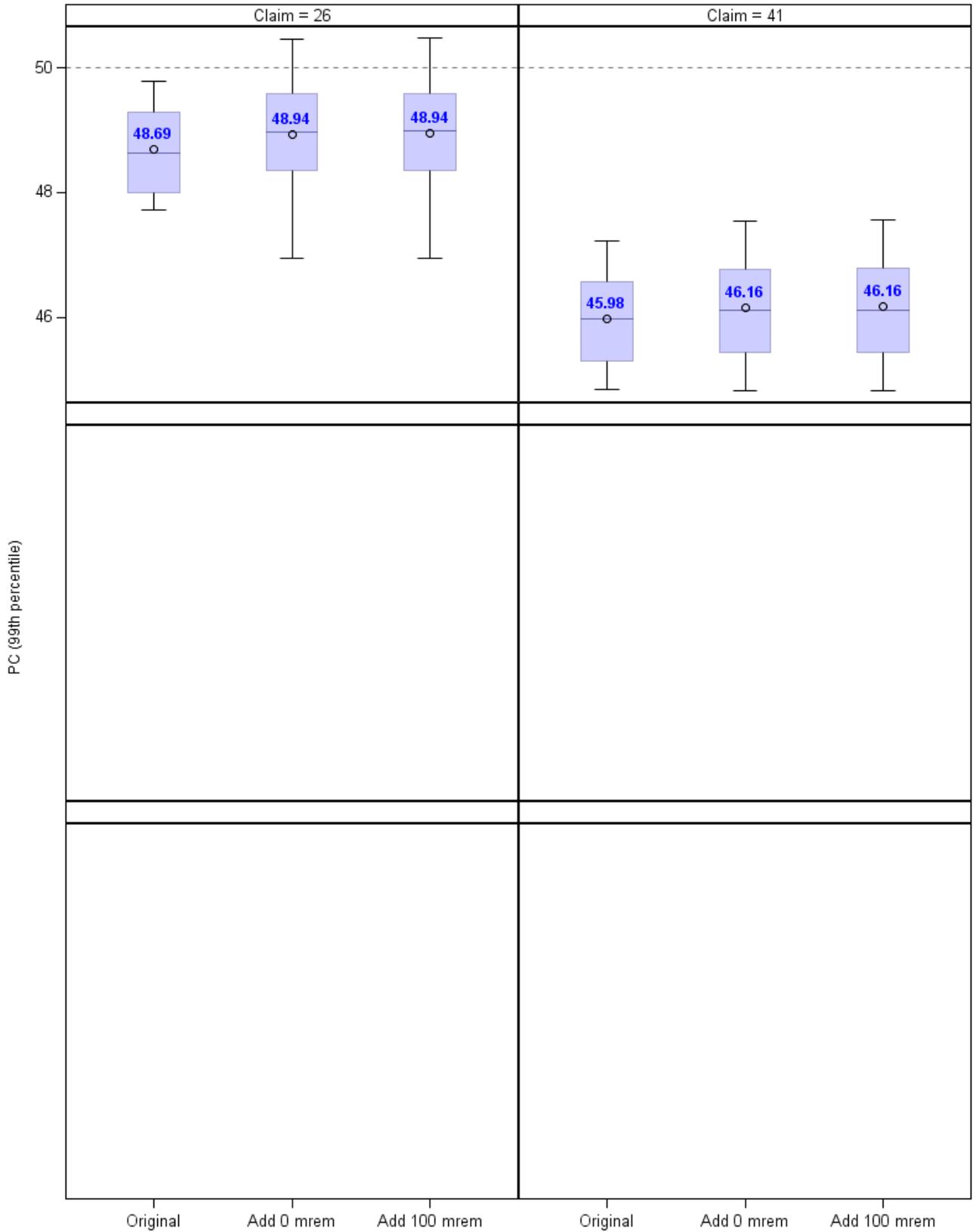
IREP Cancer Model = Non-melanoma BCC



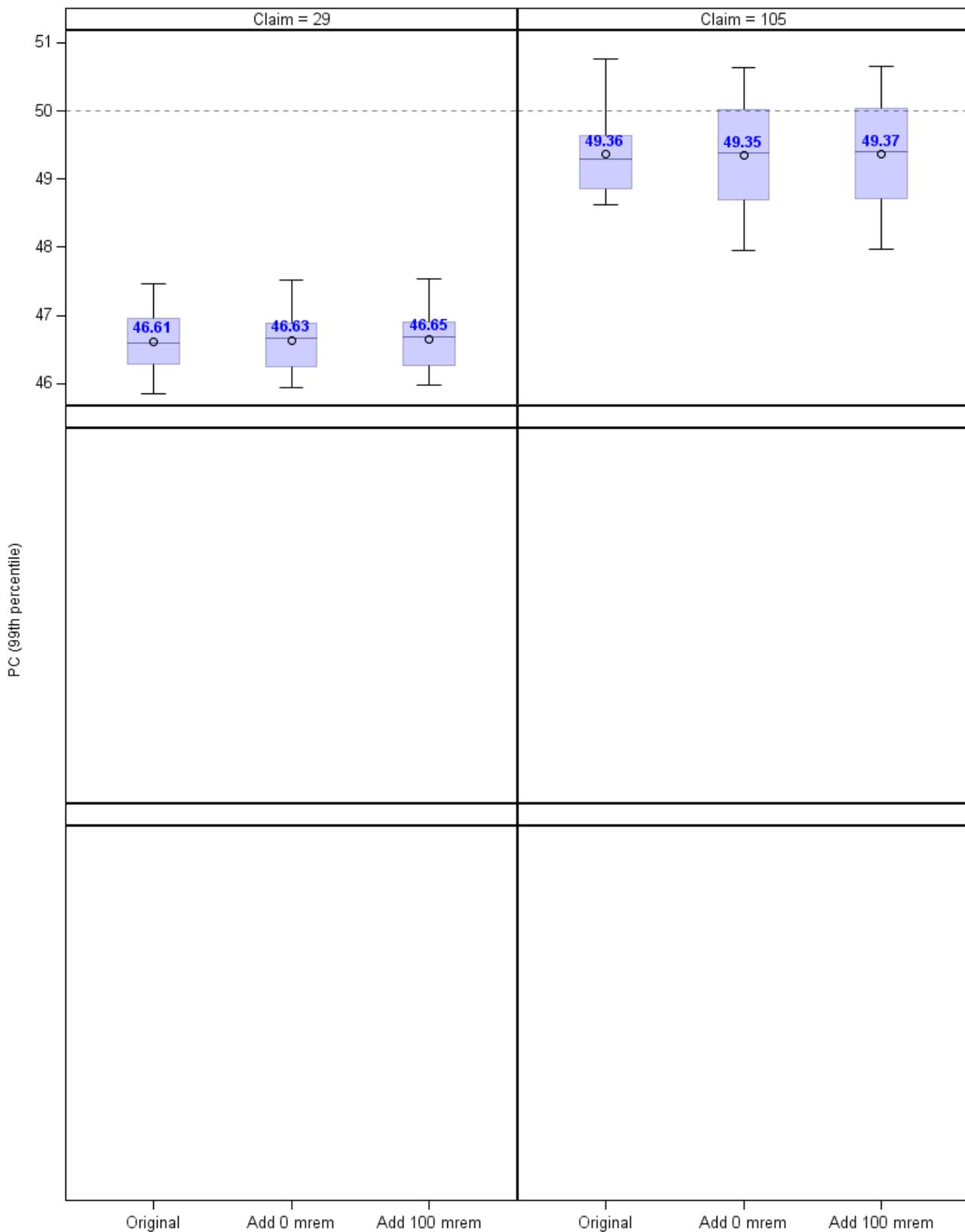
### IREP Cancer Model = Non-melanoma SCC



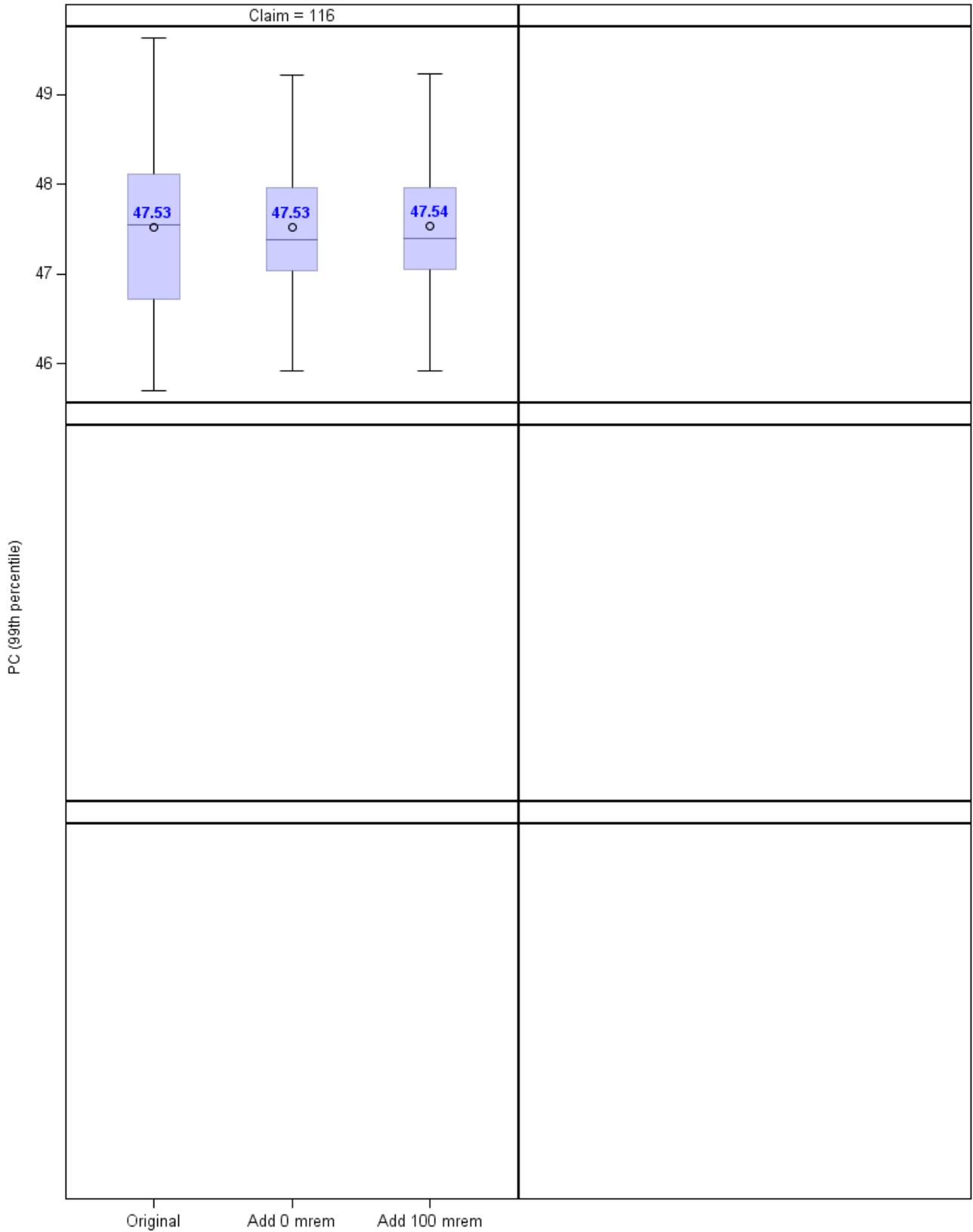
### IREP Cancer Model = Oral Cavity and Pharynx



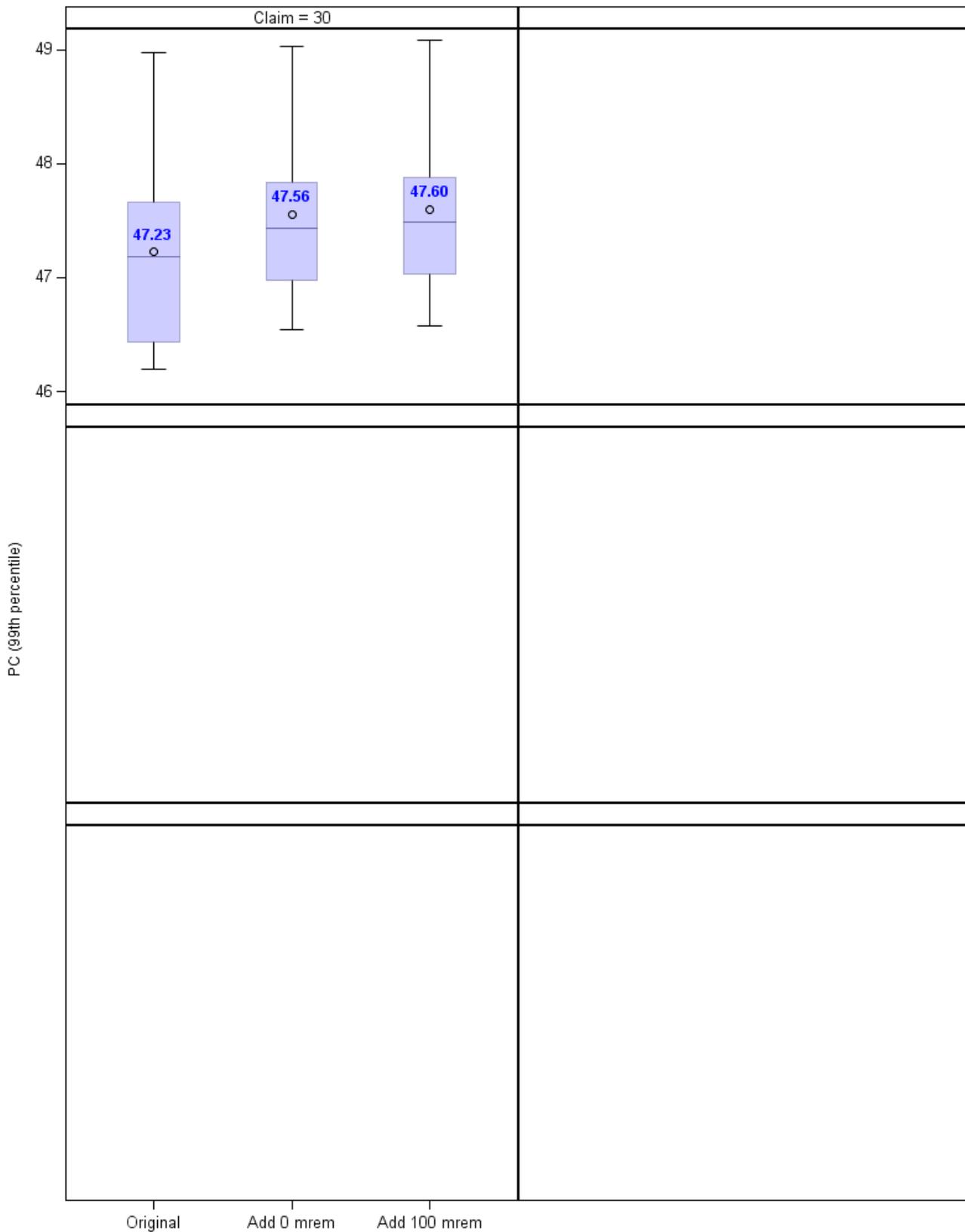
IREP Cancer Model = Other and ill-defined sites



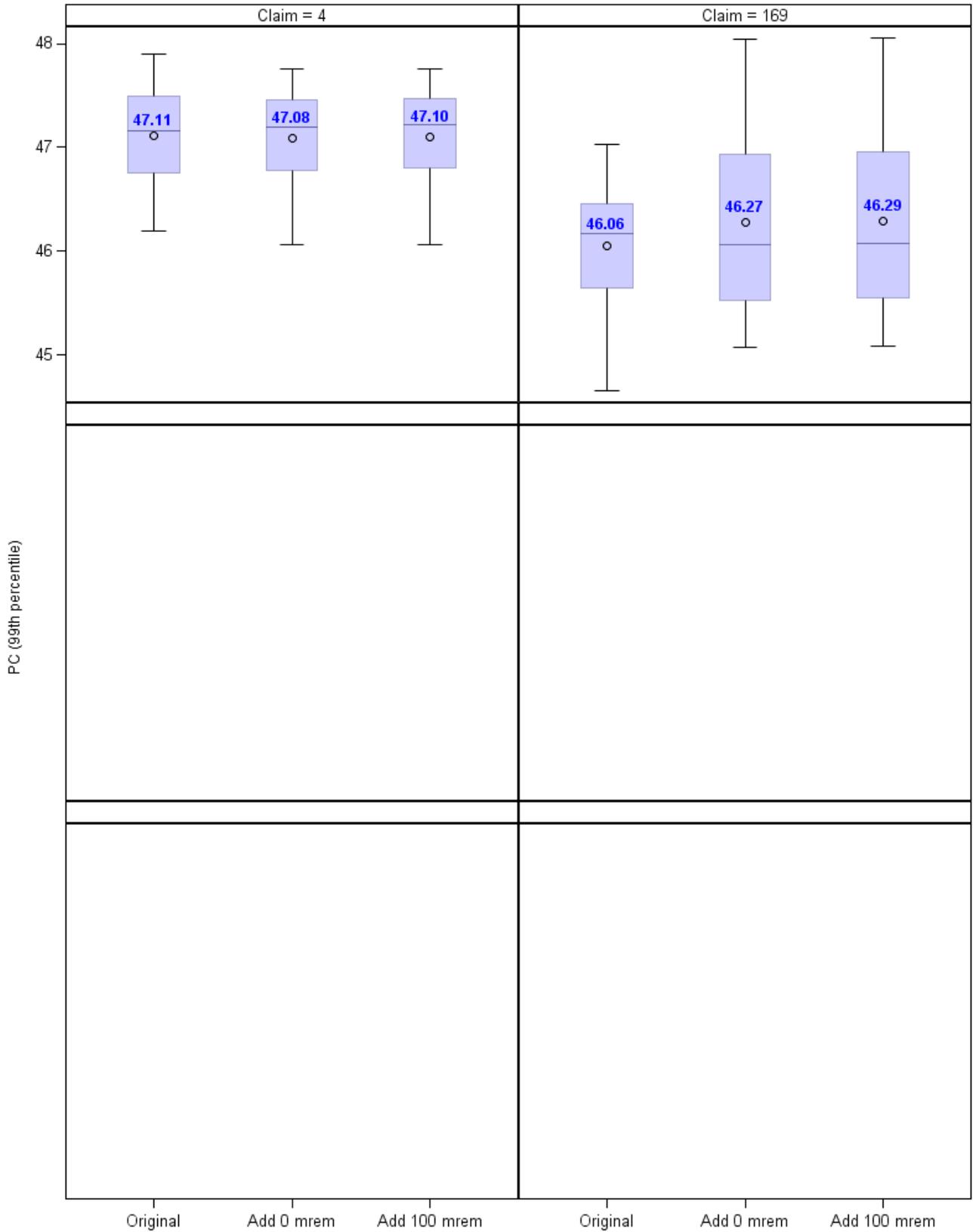
IREP Cancer Model = Other respiratory



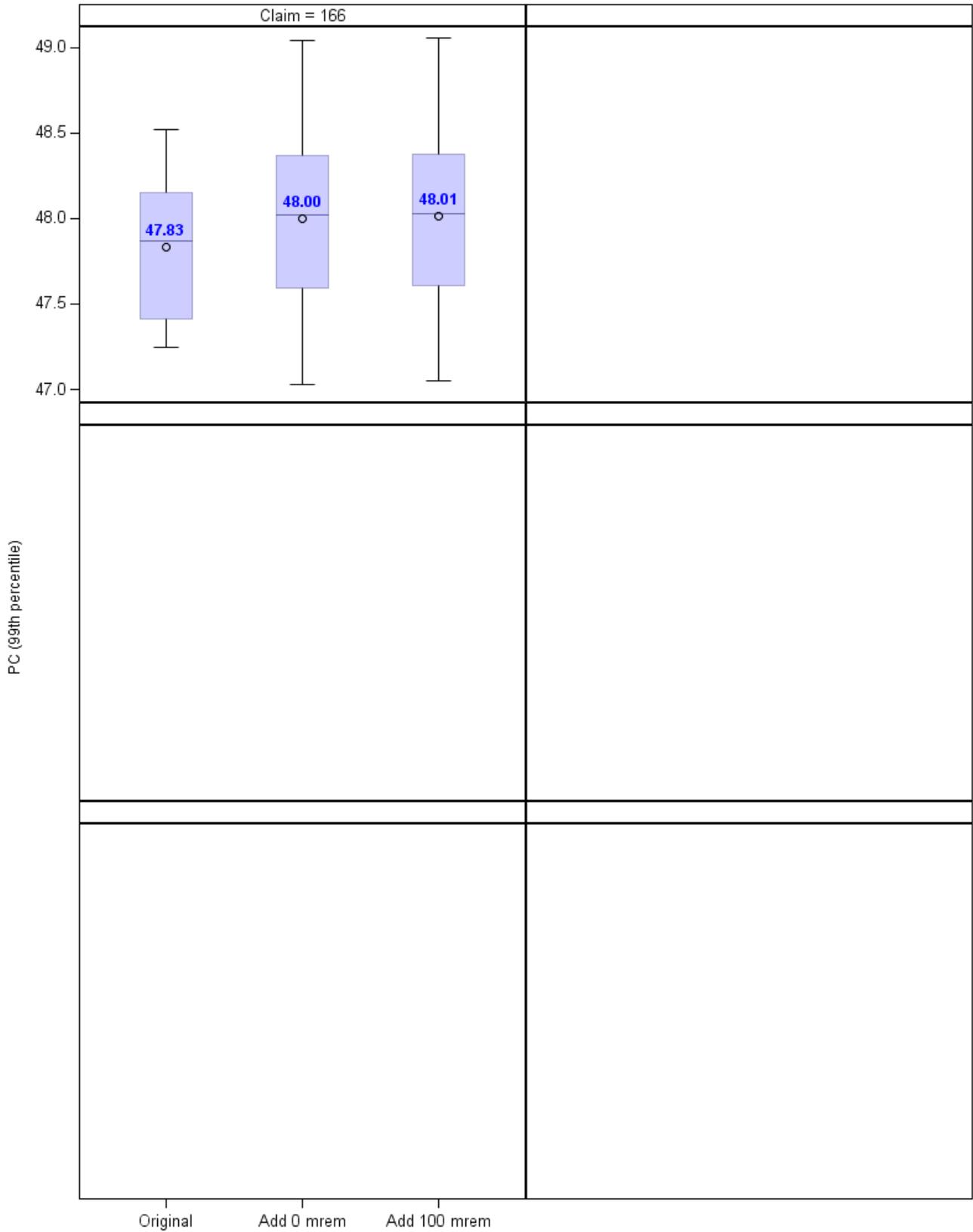
IREP Cancer Model = Ovary



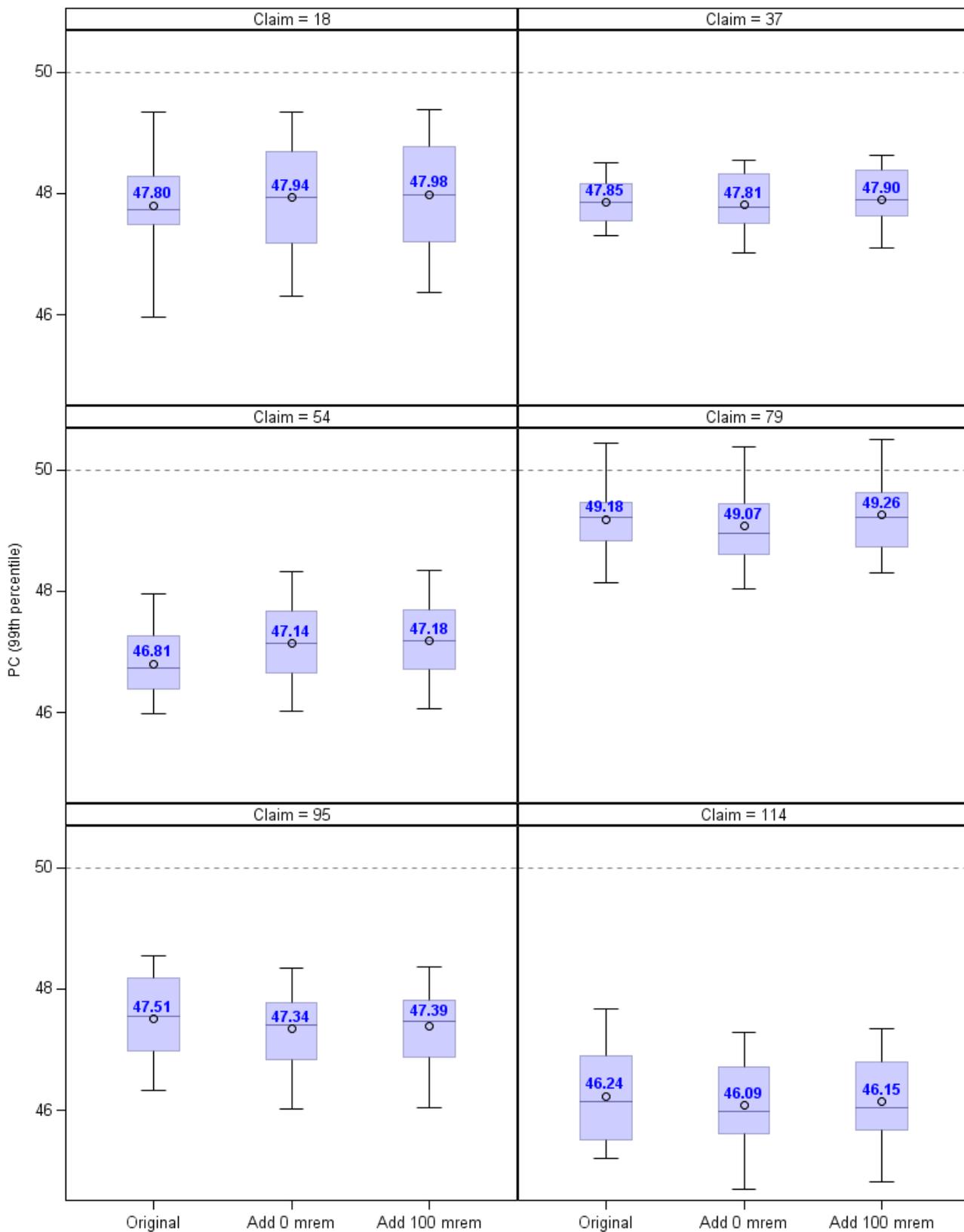
### IREP Cancer Model = Pancreas



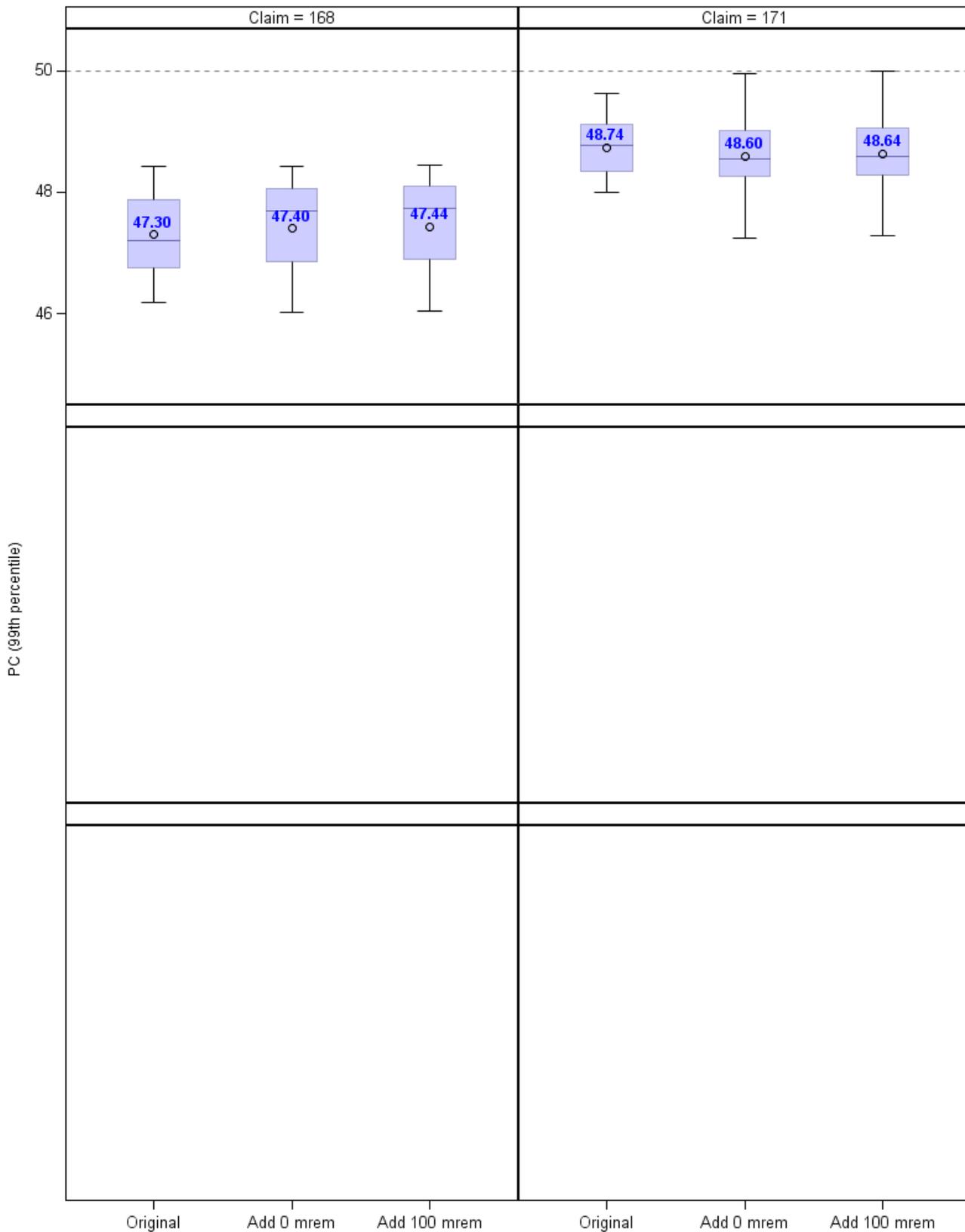
### IREP Cancer Model = Rectum



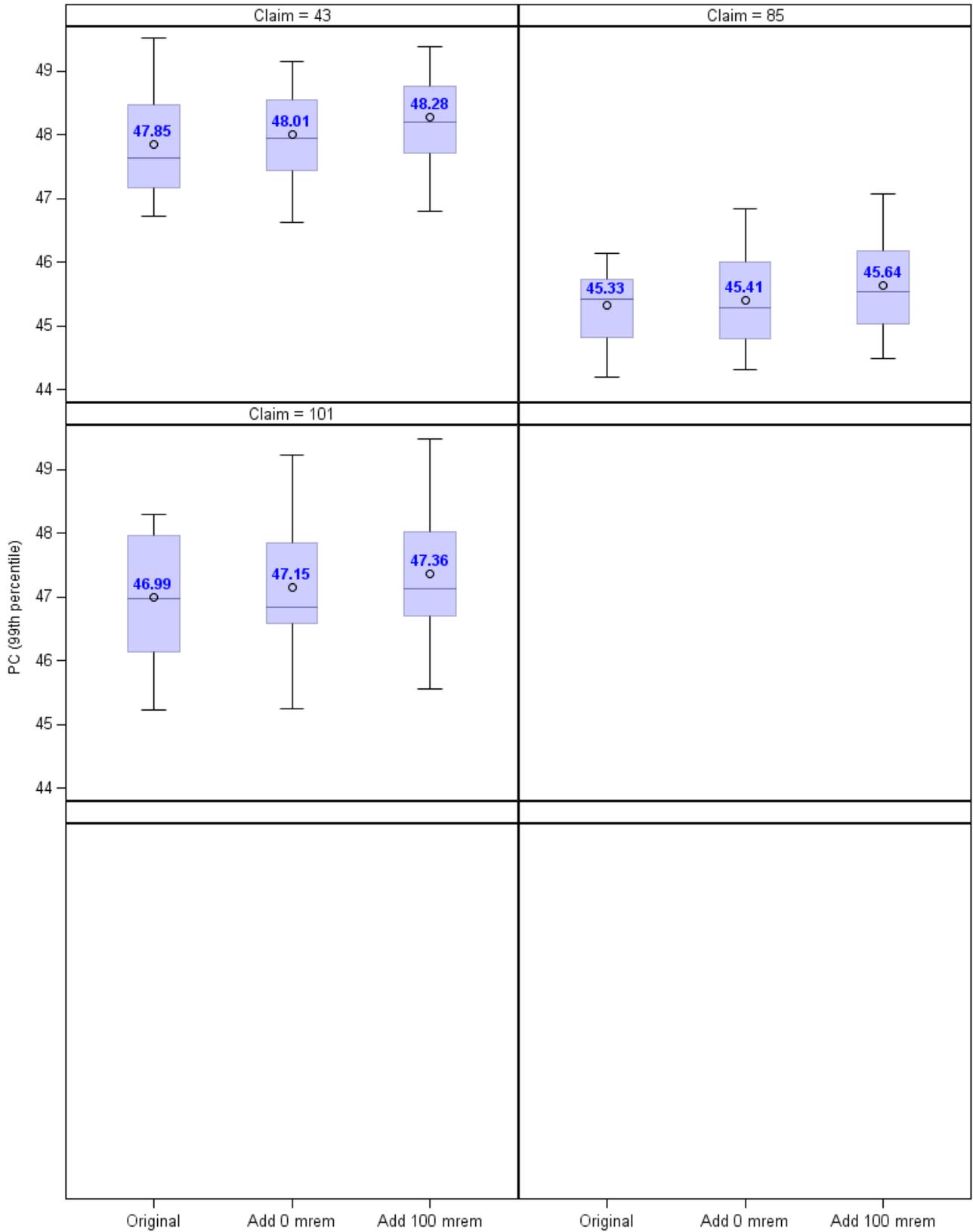
IREP Cancer Model = Stomach



### IREP Cancer Model = Stomach



IREP Cancer Model = Thyroid



IREP Cancer Model = Urinary organs (excl. bladder)

