**CHALLENGE 5**

**REPORT**

In this study, 249 mice who were identified with SCC tumors received treatment with a range of drug regimens. Over the course of 45 days, tumor development was observed and measured. The purpose of this study was to compare the performance of Pymaceuticals’ drug of interest, **Capomulin**, against the other treatment regimens.

**Introduction**:

Squamous cell carcinoma (SCC) tumor growth in mice is treated with 9 drugs in this fictitious study and a placebo regimen. The effectiveness of each drug is measured by the size of tumors in each mouse over 45 days. The size of a tumor is measured by its volume in mm3.

**Analysis**:

* In this study, 249 mice were included initially.
* 9 drug regimens were assigned to 9 groups of 25 mice each (24 in Stelasyn regimen, perhaps due to loss of a mouse (Table1b))
* One unique measurement was recorded for each mouse in one day.
* Measurements were recorded on days: 0, 5, 10, 15, 20, 25, 30, 35, 40 and 45 (10 days).

If the mice (tumors) were not measured and recorded on the days listed above, the number of measurements would < 10 (Table 1a, 1b).

* The size of tumor for every mouse on day-0 was 45 mm3.
* A drug regimen was considered effective, if the tumor reduced in size over the 45-day trial period.

**Table 1a**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **1. Capomulin** | | **2. Ceftamin** | | **3. Infubinol** | | **4. Ketapril** | | **5. Naftisol** | |
|  | Mouse ID | Read (d) | Mouse ID | Read (d) | Mouse ID | Read (d) | Mouse ID | Read (d) | Mouse ID | Read (d) |
| 1 | b128 | 10 | a275 | 10 | a203 | 10 | c832 | 10 | a818 | 10 |
| 2 | b742 | 10 | j296 | 10 | a251 | 10 | g497 | 10 | b559 | 10 |
| 3 | g288 | 10 | k210 | 10 | a685 | 10 | h246 | 10 | e213 | 10 |
| 4 | g316 | 10 | l471 | 10 | c139 | 10 | k382 | 10 | e584 | 10 |
| 5 | i557 | 10 | l661 | 10 | e476 | 10 | m550 | 10 | j755 | 10 |
| 6 | i738 | 10 | l733 | 10 | f345 | 10 | m650 | 10 | l700 | 10 |
| 7 | j119 | 10 | o287 | 10 | k483 | 10 | o331 | 10 | l725 | 10 |
| 8 | l509 | 10 | p438 | 10 | y163 | 10 | p189 | 10 | n304 | 10 |
| 9 | l897 | 10 | w151 | 10 | z581 | 10 | u327 | 10 | r604 | 10 |
| 10 | m601 | 10 | x581 | 10 | i386 | 9 | w422 | 10 | r701 | 10 |
| 11 | m957 | 10 | x822 | 10 | k804 | 8 | y260 | 10 | t724 | 10 |
| 12 | r554 | 10 | y769 | 10 | o809 | 8 | c819 | 9 | z795 | 10 |
| 13 | r944 | 10 | y865 | 10 | a577 | 7 | d474 | 9 | z969 | 10 |
| 14 | s185 | 10 | q483 | 9 | c895 | 7 | n923 | 9 | v295 | 9 |
| 15 | s710 | 10 | b759 | 7 | n671 | 7 | o973 | 9 | x264 | 9 |
| 16 | t565 | 10 | l490 | 7 | q132 | 7 | g107 | 8 | e291 | 6 |
| 17 | u364 | 10 | b487 | 6 | w584 | 7 | v603 | 8 | m133 | 6 |
| 18 | v923 | 10 | u149 | 6 | s121 | 6 | c580 | 7 | x930 | 6 |
| 19 | w914 | 10 | f436 | 4 | v719 | 5 | v289 | 6 | f993 | 5 |
| 20 | x401 | 10 | l558 | 3 | w193 | 5 | a457 | 3 | v835 | 5 |
| 21 | y793 | 10 | h531 | 2 | v766 | 4 | l264 | 3 | o725 | 4 |
| 22 | j246 | 8 | b447 | 1 | c326 | 2 | q119 | 3 | y601 | 2 |
| 23 | f966 | 5 | t573 | 1 | m756 | 2 | f278 | 2 | z234 | 2 |
| 24 | r157 | 4 | u153 | 1 | o813 | 2 | f932 | 1 | v199 | 1 |
| 25 | w150 | 3 | x226 | 1 | v339 | 2 | h428 | 1 | x336 | 1 |

**Table 1b**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **6. Placebo** | | **7. Propriva** | | **8. Ramicane** | | **9. Stelasyn** | | **10. Zoniferol** | |
|  | Mouse ID | Read (d) | Mouse ID | Read (d) | Mouse ID | Read (d) | Mouse ID | Read (d) | Mouse ID | Read (d) |
| 1 | a262 | 10 | a699 | 10 | a411 | 10 | a492 | 10 | a401 | 10 |
| 2 | a897 | 10 | g570 | 10 | a444 | 10 | a963 | 10 | c264 | 10 |
| 3 | c282 | 10 | i635 | 10 | a520 | 10 | b879 | 10 | c302 | 10 |
| 4 | c757 | 10 | o562 | 10 | a644 | 10 | c402 | 10 | c559 | 10 |
| 5 | c766 | 10 | t198 | 10 | c758 | 10 | i901 | 10 | f545 | 10 |
| 6 | e227 | 10 | v991 | 10 | d251 | 10 | j984 | 10 | g296 | 10 |
| 7 | o795 | 10 | w350 | 10 | e662 | 10 | k862 | 10 | j365 | 10 |
| 8 | q787 | 10 | c927 | 9 | g791 | 10 | m269 | 10 | k894 | 10 |
| 9 | t718 | 10 | g558 | 9 | i177 | 10 | s565 | 10 | o926 | 10 |
| 10 | x773 | 10 | r107 | 7 | i334 | 10 | t451 | 10 | p136 | 10 |
| 11 | y478 | 10 | s141 | 7 | j913 | 10 | x402 | 10 | q511 | 10 |
| 12 | n763 | 9 | s187 | 7 | j989 | 10 | p387 | 9 | q633 | 10 |
| 13 | q582 | 8 | p310 | 6 | k403 | 10 | f234 | 8 | s337 | 10 |
| 14 | w167 | 8 | k603 | 5 | m546 | 10 | p981 | 8 | w575 | 10 |
| 15 | o302 | 7 | u946 | 5 | n364 | 10 | w697 | 8 | a788 | 7 |
| 16 | i669 | 6 | l215 | 3 | q597 | 10 | a366 | 7 | b313 | 6 |
| 17 | s152 | 6 | n678 | 3 | r811 | 10 | h333 | 7 | k754 | 5 |
| 18 | j235 | 5 | o523 | 3 | s508 | 10 | w540 | 6 | f129 | 4 |
| 19 | t994 | 5 | x111 | 3 | u196 | 10 | k510 | 5 | m331 | 4 |
| 20 | r850 | 4 | x209 | 3 | z578 | 10 | g867 | 4 | n967 | 4 |
| 21 | i477 | 3 | z435 | 3 | q610 | 8 | v764 | 4 | x613 | 4 |
| 22 | s166 | 3 | n630 | 2 | c458 | 7 | s619 | 2 | d164 | 3 |
| 23 | v409 | 3 | w746 | 2 | r921 | 7 | z314 | 2 | f394 | 2 |
| 24 | v989 | 3 | n482 | 1 | y449 | 4 | o848 | 1 | w140 | 2 |
| 25 | l872 | 1 | **g989** | **13** | w678 | 2 |  |  | d133 | 1 |

Of the 249 mice the recording ‘Timepoint’ for one mouse (g989) showed inconsistencies (Table 2).

There are duplicate measurements recorded for days: 0, 5, 10, 15, 20. The total number records for tumor measurements is 13, although the number should not exceed 10.

Since only 1 measurement per day is considered in this study, data for ‘Mouse ID’: g989 was eliminated, and 248 mice remained as subjects of the study.

**Table 2**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Mouse ID** | **Timepoint**  **(days)** | **Tumor Volume (mm3)** | **Drug Regimen** |
| 1 | g989 | 0 | 45.0 | Propriva |
| 2 | g989 | 0 | 45.0 | Propriva |
| 3 | g989 | 5 | 48.8 | Propriva |
| 4 | g989 | 5 | 47.6 | Propriva |
| 5 | g989 | 10 | 51.7 | Propriva |
| 6 | g989 | 10 | 49.9 | Propriva |
| 7 | g989 | 15 | 51.3 | Propriva |
| 8 | g989 | 15 | 53.4 | Propriva |
| 9 | g989 | 20 | 55.3 | Propriva |
| 10 | g989 | 20 | 54.7 | Propriva |
| 11 | g989 | 25 | 56.0 | Propriva |
| 12 | g989 | 30 | 59.1 | Propriva |
| 13 | g989 | 35 | 62.6 | Propriva |

Graph 1 shows the total number of times tumor(s) were measured for each drug regimen. Capomulin and Ramicane regimens included the highest number of measurements for the size of tumors. The lowest number of measurements were for the regimen for Propriva.

**Graph 1**

A graph of a number of drugs

Description automatically generated

This may provide a **preliminary indication** of the effectiveness of a drug. The fewer number of measurements might indicate tumor-growth rather than tumor-shrinkage and consequently, loss of mice.

**Graph 2**

A diagram of a number of boxes with different colored lines

Description automatically generated

Box plots in Graph 2 show the final reading on tumor sizes recorded on day 45 for 4 drug regimens, *viz.*, Capomulin, Ramicane, Infubinol and Ceftamin. The smaller values of tumor sizes ranging between 30 and 40 mm3 shows the effectiveness of the drugs **Capomulin** and **Ramicane**. In comparison, final tumor sizes in the range of ~50 - 65 mm3 for drug regimens **Infubinol** and **Ceftamin** shows that these two drugs may not be effective in treating SCC.

The red dot is a small collection of outliers for the drug regimen Infubinol. The importance of outliers cannot be explained in the context of the present data. Since most of the measurements in this regimen of Infubinol show tumor growth, this drug may be considered ineffective. Thus, the significance of **outliers (31mm3, 36mm3)** may not be pursued further.

The **orange line** within each box in Graph 2 is the **median** value of tumor size for each drug regimen.

Table 2 illustrates the statistical summary of tumor volumes for all regimens, including Placebo. This data assumes that the data for each regimen taken over 45 days has **‘normal’ distribution**.

The two drug regimens showing the **best results, Capomulin** and **Ramicane** have the lowest median values of 41.6 mm3 and 40.7 mm3, respectively. The standard deviations, or the dispersion of data points is also the lowest, 5.0 mm3 and 4.8 mm3, respectively.

All **other regimens** show their medians and standard deviations as values close to those observed by the placebo regimen. Hence, the emergence of **Capomulin** and **Ramicane** as the two most effective drugs.

**Table 2**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Tumor Volume (mm3) | | | |
| Drug Regimen | Mean | Median | Variance | Standard  Deviation |
| Capomulin | 40.7 | 41.6 | 24.9 | 5.0 |
| Ceftamin | 52.6 | 51.8 | 39.3 | 6.3 |
| Infubinol | 52.9 | 51.8 | 43.1 | 6.6 |
| Ketapril | 55.2 | 53.7 | 68.6 | 8.3 |
| Naftisol | 54.3 | 52.5 | 66.2 | 8.1 |
| Placebo | 54.0 | 52.3 | 61.2 | 7.8 |
| Propriva | 52.3 | 50.4 | 43.9 | 6.6 |
| Ramicane | 40.2 | 40.7 | 23.5 | 4.8 |
| Stelasyn | 54.2 | 52.4 | 59.5 | 7.7 |
| Zoniferol | 53.2 | 51.8 | 48.5 | 7.0 |

**Graph 3**

A graph with a line and a line

Description automatically generated

Graph 3 displays tumor volumes on one specific subject, ‘Mouse ID’: *l*509over 45 days, while undergoing the **Capomulin** therapy treatment. The tumor showed a gradual increase in size over the first 20 days followed by sharp reduction in size over the next 15 days, and a subsequent increase at the same rate as in the initial period.

In Graph 4 the relationship between **tumor sizes** in mice subjected to **Capomulin** regimen and their **weights**, is explored. The correlation is positive. Pearson Correlation Coefficient, ***r* = 0.84**, implying a strong correlation between the average size of tumor and the weight of the mouse receiving the therapeutic drug.

The linear regression line shows a slope (0.95 mm3/g), nearly equal to 1, indicating a positive **linear relationship of proportionality** between the tumor size and weight of a mouse.

**Graph 4**



A graph with a red line

Description automatically generated

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Data obtained in this study favors the performance of **Capomulin regimen** to all other drug regimen used.

The following graphs illustrate the reasoning behind the hypothesis.

Graph 5 is a line graph for each drug therapy. The average tumor size decreased over time for only two regimens, Capomulin and Ramicane.

For all other regimens, the average tumor size increased, and in 2 cases, performances were worse than the placebo regimen. Hence the preference for Capomulin and Ramicane regimens in SCC treatment.

Graph 5

A graph of different colored lines

Description automatically generated

Graph 6 isolates **four drug regimens** that performed better than the placebo regimen. These 4 regimens are represented in the box plots in Graph 2.

Graph 6

A graph of a drug regimen

Description automatically generated

Graph 7 shows the selection of Capomulin and Ramicane, and illustrating clearly, the shrinking of tumors over a period of 45 days.

From the graph it appears that Ramicane may be a better performer of the two.

Ramicane regimen reduced the average size of tumor faster (blue line) up to day 25.

The tumors reduced in size significantly, lower than in Capomulin regimen. After day 25, however, the sizes began to increase and became equal to the average size of tumors treated by the Capomulin regimen on day 30, followed again by size reduction.

While the rapid reduction in tumor size is the desired outcome of the treatment, the subsequent increase is not.

**Capomulin** regimen, in the other hand, shows a constant and consistent reduction in tumor sizes. This trend in reduction of tumor sizes makes this drug regimen **more reliable** than Ramicane treatment.

**Graph 7**

A graph of a drug regimen

Description automatically generated

Finally, the study included 51% male mice and 49% female mice, as shown below:

A blue and orange pie chart

Description automatically generated

Graph 8 shows the effect of the two best regimen on the **male** and **female** subjects of the study.

**Graph 8**

A graph with colored lines and dots

Description automatically generated

The **Ramicane** regimen benefitted the male population more than it did female population.

The average tumor size in **male** population showed rapid reduction, followed by slow reduction, and followed by rapid reduction again. Unlike male population, tumor size in the **female** population showed and increase, followed by reduction at the same rate as in Capomulin regimen.

Whereas the **Capomulin** treatment benefitted both **male** and **female** populations equally. The rate of tumor reduction in size was constant.

**Conclusion**:

Capomulin regimen demonstrates that the average tumor size can be reduced **consistently** and at a **constant rate**.

**Its predictability makes this regimen more reliable compared to Ramicane regimen.**

The data and its visualization provide evidence in favor of Capomulin regiment, as the most reliable option among all the drug therapies included in this study.