```python
import numpy as np
import pandas as pd
import seaborn as sns
from xgboost import XGBClassifier
from sklearn.model_selection import cross_val_score, StratifiedKFold, cross_val
from sklearn.metrics import confusion_matrix, roc_auc_score, fbeta_score,precis
from tqdm.notebook import tqdm
from sklearn.model_selection import ParameterGrid
from sklearn.feature_selection import SelectKBest, mutual_info_classif
from imblearn.pipeline import Pipeline
from imblearn.over_sampling import SMOTE
import matplotlib.pyplot as plt
```

```python
from google.colab import drive
drive.mount('/content/drive')
```

```
Mounted at /content/drive
```

```
path = '/content/drive/MyDrive/modelowanie/projekt/combined_data.csv'
df = pd.read_csv(path)

#HER2-neg
df = df[df['characteristics_ch1_4'].astype(str).str.strip().str.endswith("N")].

#data preprocessing
df.drop(columns=['title'], inplace=True)
geo_col = ['geo_accession']
characteristics_cols = [col for col in df.columns if 'characteristics' in col.l
other_cols = [col for col in df.columns if 'characteristics' not in col.lower()


#clinical
df_meta = df[geo_col + characteristics_cols]
df_meta.set_index("geo_accession", inplace=True)
df_meta = df_meta.copy()
new_column_names = [str(el).split(':')[0].strip() for el in df_meta.iloc[0, :]]
df_meta.columns = new_column_names

for col in df_meta.columns:
    df_meta[col] = df_meta[col].astype(str).str.split(':').str[-1].str.strip()

#expresion
df_gene_expression = df[geo_col + other_cols]
df_gene_expression.set_index("geo_accession", inplace=True)
df_gene_expression_clean = df_gene_expression.loc[:, ~df_gene_expression.columr

df_expr_final = df_gene_expression_clean.T

#final check
common_samples = df_expr_final.columns.intersection(df_meta.index)
df_expr_final = df_expr_final[common_samples]
df_meta_final = df_meta.loc[common_samples]
df_expr_final.index.name = 'gene'

print(f"Expresion matrix: {df_expr_final.shape} (genes × probes)")
print(f"Clinical data: {df_meta.shape} (probes × characteristics)")
```

```
/tmp/ipython-input-3-2644258436.py:2: DtypeWarning: Columns (0) have mixed
  df = pd.read_csv(path)
Expresion matrix: (22215, 485) (genes × probes)
Clinical data: (485, 20) (probes × characteristics)
```

```
df_meta_final['pathologic_response_pcr_rd'].unique()
```

```
array(['RD', 'pCR', 'NA', 'RCB-II', 'RCB-III', 'RCB-0/I'], dtype=object)
```

TUNNING

```
def tune_xgboost_hyperparams_withtqdm(X, y, scale_pos_weight=None, cv=5, scoring

    param_grid = {
        "max_depth": [3, 5, 7],
        "learning_rate": [0.01, 0.05, 0.1, 0.2],
        "n_estimators": [100, 200, 300],
        "colsample_bytree": [0.6, 0.8, 1.0],
        "min_child_weight": [1, 3, 5]
    }


    grid = list(ParameterGrid(param_grid))
    best_score = -1
    best_params = None

    print(f"Tuning ({len(grid)} combinantions, cv={cv})")

    for params in tqdm(grid, desc="Tuning (f2)", leave=True):
        scores = []
        skf = StratifiedKFold(n_splits=cv, shuffle=True, random_state=42)

        for train_idx, test_idx in skf.split(X, y):
            X_train, X_test = X.iloc[train_idx], X.iloc[test_idx]
            y_train, y_test = y.iloc[train_idx], y.iloc[test_idx]

            model = XGBClassifier(
                tree_method="hist",
                device="cuda",
                eval_metric="logloss",
                random_state=42,
                **params
            )
            model.fit(X_train, y_train)
            y_pred = model.predict(X_test)
            scores.append(fbeta_score(y_test, y_pred, beta=2))

        mean_score = sum(scores) / len(scores)

        if mean_score > best_score:
            best_score = mean_score
            best_params = params

    print("\nBest params:")
    for k, v in best_params.items():
        print(f"{k}: {v}")
    print(f"Best {scoring}: {best_score:.3f}")

    return best_params
```

DLA ER-

```
def analyze_er_withgrid_1(er_status_value, df_meta_final, df_expr_final,
                           top_n_genes=100, threshold=0.05, test_size=0.2, cv=5

    #filtering data
    valid_labels = ["pCR", "RCB-0", "RCB-I", "RCB-0/I", "RD", "RCB-II", "RCB-II
    meta = df_meta_final[
        (df_meta_final["er_status_ihc"] == er_status_value) &
        (df_meta_final["pathologic_response_pcr_rd"].isin(valid_labels))
    ].copy()

    #0/1 label
    meta["pCR_label"] = meta["pathologic_response_pcr_rd"].isin(["pCR", "RCB-0"

    if verbose:
        print(f"\n Analysis for ER{er_status_value}")
        print(f"Amount of probes: {meta.shape[0]}")
        print(f"(0=RD, 1=pCR):\n{meta['pCR_label'].value_counts()}\n")

    expr = df_expr_final[meta.index].T
    y = meta["pCR_label"]

    #Train and test data
    train_indices, test_indices = train_test_split(
        meta.index,
        test_size=test_size,
        stratify=y,
        random_state=42
    )

    X_train_full = expr.loc[train_indices]
    y_train_full = y.loc[train_indices]

    X_test = expr.loc[test_indices]
    y_test = y.loc[test_indices]

    if verbose:
        print(f"Train dataset:")
        print(y_train_full.value_counts())
        print(f"Test dataset:")
        print(y_test.value_counts())

    #Gene seleciton and training
    selector = SelectKBest(mutual_info_classif, k=top_n_genes)
    selector.fit(X_train_full, y_train_full)
    top_genes = X_train_full.columns[selector.get_support()]

    X_train = X_train_full[top_genes]
    X_test = X_test[top_genes]
```

```
smote_sampler = SMOTE(random_state=42)

if use_tuning:
    best_params = tune_xgboost_hyperparams_withtqdm(X_train, y_train_full,
    xgb_model = XGBClassifier(
        tree_method="hist",
        device="cuda",
        eval_metric="logloss",
        random_state=42,
        **best_params
    )
else:
    xgb_model = XGBClassifier(
        tree_method="hist",
        device="cuda",
        eval_metric="logloss",
        random_state=42
    )

model_pipeline = Pipeline([
    ('sampler', smote_sampler),
    ('classifier', xgb_model)
])

model_pipeline.fit(X_train, y_train_full)
y_proba_test = model_pipeline.predict_proba(X_test)[:, 1]
y_pred_test = (y_proba_test >= threshold).astype(int)

#Metrics
cm = confusion_matrix(y_test, y_pred_test)
tn, fp, fn, tp = cm.ravel()
roc_auc = roc_auc_score(y_test, y_proba_test)
acc = (tp + tn) / cm.sum()
sens = tp / (tp + fn) if (tp + fn) > 0 else 0
spec = tn / (tn + fp) if (tn + fp) > 0 else 0
ppv = tp / (tp + fp) if (tp + fp) > 0 else 0
npv = tn / (tn + fn) if (tn + fn) > 0 else 0
bal_acc = (sens + spec) / 2

if verbose:
    grupa = "ER+" if er_status_value == "P" else "ER-"
    print(f"\nResults for (top {top_n_genes} genes) for {grupa}")
    print("Confusion matrix:")
    print(cm)
    print(f"AUC:                 {roc_auc:.2f}")
    print(f"Accuracy:            {acc:.2f}")
    print(f"Sensitivity (Recall):{sens:.2f}")
    print(f"Specificity:         {spec:.2f}")
    print(f"PPV (Precision):     {ppv:.2f}")
    print(f"NPV:                 {npv:.2f}")
```

```
        print(f"Balanced Accuracy:   {bal_acc:.2f}")

    return {
        "group": "ER+" if er_status_value == "P" else "ER-",
        "top_genes": top_genes,
        "AUC": roc_auc,
        "Accuracy": acc,
        "Sensitivity": sens,
        "Specificity": spec,
        "PPV": ppv,
        "NPV": npv,
        "Balanced_Accuracy": bal_acc,
        "y_true": y_test,
        "y_proba": y_proba_test,
        "y":y
    }
```

bez smote

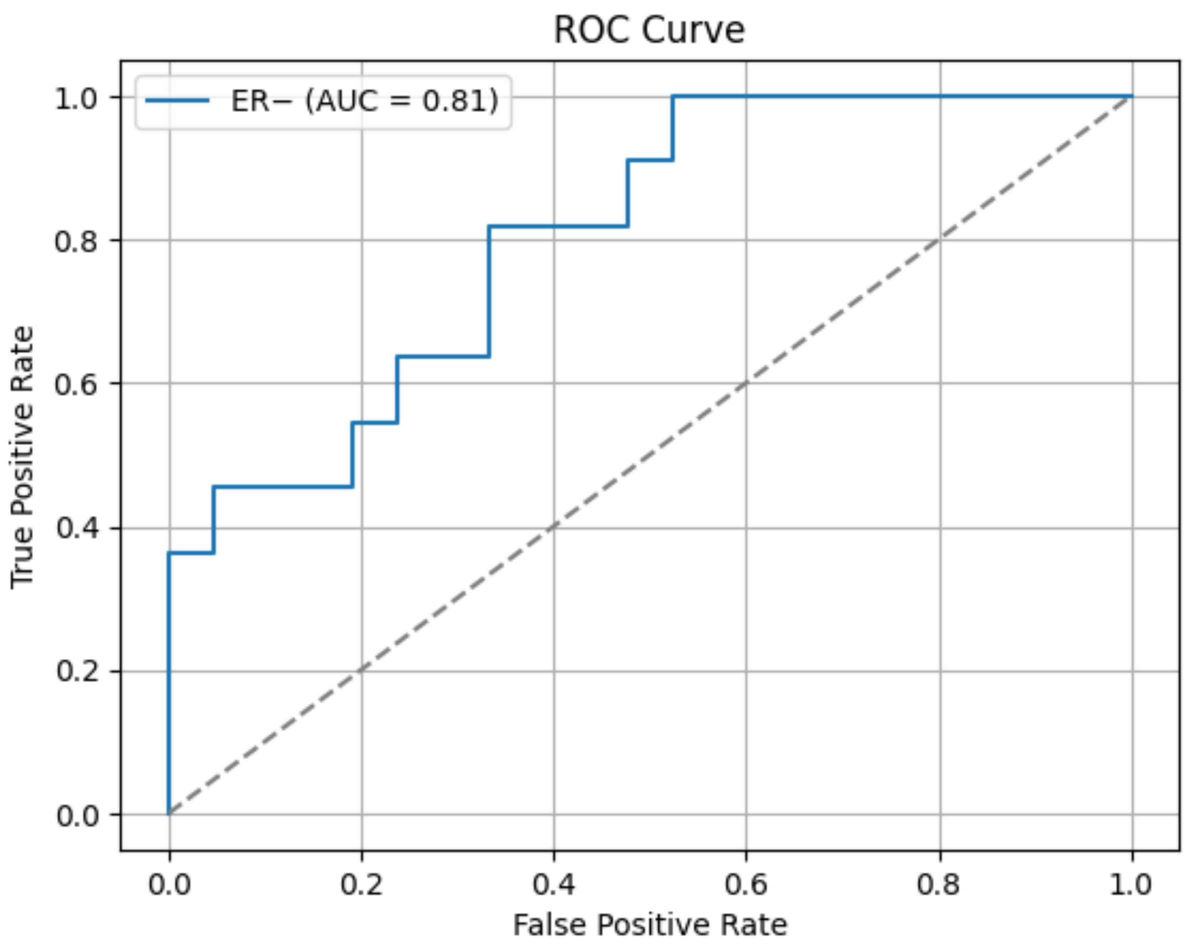
```
def analyze_er_withgrid_1_no_smote(er_status_value, df_meta_final, df_expr_fina
                           top_n_genes=100, threshold=0.5, test_size=0.2, cv=5,

    #filtering data
    valid_labels = ["pCR", "RCB-0", "RCB-I", "RCB-0/I", "RD", "RCB-II", "RCB-II
    meta = df_meta_final[
        (df_meta_final["er_status_ihc"] == er_status_value) &
        (df_meta_final["pathologic_response_pcr_rd"].isin(valid_labels))
    ].copy()

    #0/1 label
    meta["pCR_label"] = meta["pathologic_response_pcr_rd"].isin(["pCR", "RCB-0"

    if verbose:
        print(f"\n Analysis for ER{er_status_value}")
        print(f"Amount of probes: {meta.shape[0]}")
        print(f"(0=RD, 1=pCR):\n{meta['pCR_label'].value_counts()}\n")

    expr = df_expr_final[meta.index].T
    y = meta["pCR_label"]

    #Train and test data
    train_indices, test_indices = train_test_split(
        meta.index,
        test_size=test_size,
        stratify=y,
        random_state=42
    )

    X_train_full = expr.loc[train_indices]
    y_train_full = y.loc[train_indices]

    X_test = expr.loc[test_indices]
    y_test = y.loc[test_indices]

    if verbose:
        print(f"Train dataset:")
        print(y_train_full.value_counts())
        print(f"Test dataset:")
        print(y_test.value_counts())


    #Gene seleciton and training
    selector = SelectKBest(mutual_info_classif, k=top_n_genes)
    selector.fit(X_train_full, y_train_full)
    top_genes = X_train_full.columns[selector.get_support()]

    X_train = X_train_full[top_genes]
    X_test = X_test[top_genes]


    if use_tuning:
        best_params = tune_xgboost_hyperparams_withtqdm(X_train, y_train_full,
        xgb_model = XGBClassifier(
            tree_method="hist",
            device="cuda",
            eval_metric="logloss",
            random_state=42,
            **best_params
        )
    else:
        xgb_model = XGBClassifier(
            tree_method="hist",
            device="cuda",
            eval_metric="logloss",
            random_state=42
        )

    model_pipeline = Pipeline([
        ('classifier', xgb_model)
    ])

    model_pipeline.fit(X_train, y_train_full)
    y_proba_test = model_pipeline.predict_proba(X_test)[:, 1]
    y_pred_test = (y_proba_test >= threshold).astype(int)


    #Metrics
    cm = confusion_matrix(y_test, y_pred_test)
    tn, fp, fn, tp = cm.ravel()
    roc_auc = roc_auc_score(y_test, y_proba_test)
    acc = (tp + tn) / cm.sum()
    sens = tp / (tp + fn) if (tp + fn) > 0 else 0
    spec = tn / (tn + fp) if (tn + fp) > 0 else 0
    ppv = tp / (tp + fp) if (tp + fp) > 0 else 0
    npv = tn / (tn + fn) if (tn + fn) > 0 else 0
    bal_acc = (sens + spec) / 2


    if verbose:
        grupa = "ER+" if er_status_value == "P" else "ER-"
        print(f"\nResults for (top {top_n_genes} genes) for {grupa}")
        print("Confusion matrix:")
        print(cm)
        print(f"AUC:                 {roc_auc:.2f}")
        print(f"Accuracy:            {acc:.2f}")
        print(f"Sensitivity (Recall):{sens:.2f}")
        print(f"Specificity:         {spec:.2f}")
        print(f"PPV (Precision):     {ppv:.2f}")
        print(f"NPV:                 {npv:.2f}")
        print(f"Balanced Accuracy:   {bal_acc:.2f}")

    return {
        "group": "ER+" if er_status_value == "P" else "ER-",
        "top_genes": top_genes,
        "AUC": roc_auc,
        "Accuracy": acc,
        "Sensitivity": sens,
        "Specificity": spec,
        "PPV": ppv,
        "NPV": npv,
        "Balanced_Accuracy": bal_acc,
        "y_true": y_test,
        "y_proba": y_proba_test,
        "y":y
    }


print("Analyzing ER- group with tuning")
results_er_negative_with_tune = analyze_er_withgrid_1(
    er_status_value="N",
    df_meta_final=df_meta_final,
    df_expr_final=df_expr_final,
    top_n_genes=100,
    threshold=0.21,
    test_size=0.2,
    use_tuning=True,
    cv=4,
    verbose=True
)

print(f"\nAnalyzing ER- group with tuning, without SMOTE")
```

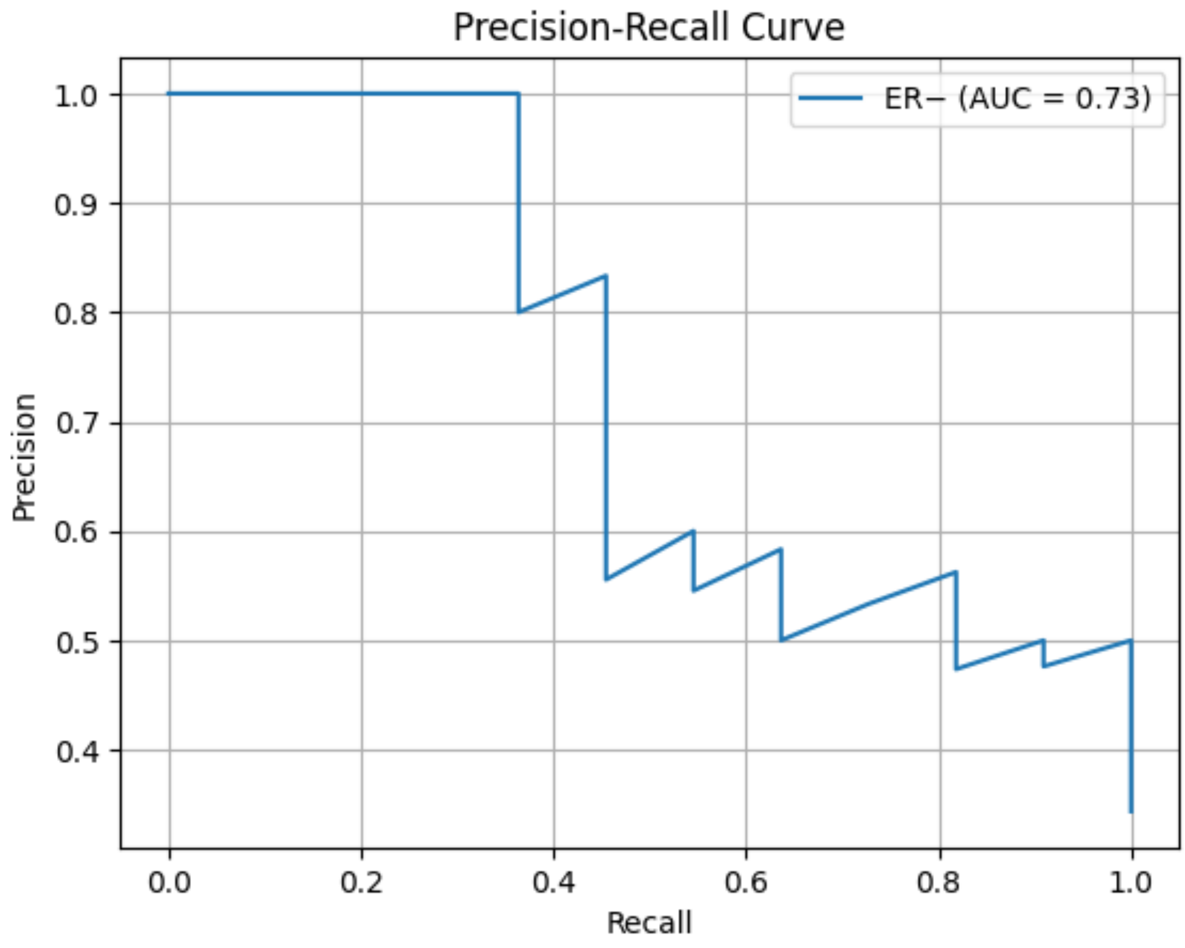
```
results_er_negative_with_tune_no_smote = analyze_er_withgrid_1_no_smote(
    er_status_value="N",
    df_meta_final=df_meta_final,
    df_expr_final=df_expr_final,
    top_n_genes=100,
    threshold=0.21,
    test_size=0.2,
    use_tuning=True,
    cv=4,
    verbose=True
)
```

```
Analyzing ER- group with tuning

 Analysis for ERN
Amount of probes: 159
(0=RD, 1=pCR):
pCR_label
0    104
1     55
Name: count, dtype: int64

Train dataset:
pCR_label
0    83
1    44
Name: count, dtype: int64
Test dataset:
pCR_label
0    21
1    11
Name: count, dtype: int64
Tuning (324 combinantions, cv=4)
Tuning (f2): 100%                                324/324 [06:07<00:00,  1.08it/s]

Best params:
colsample_bytree: 1.0
learning_rate: 0.2
max_depth: 3
min_child_weight: 1
n_estimators: 100
Best f2: 0.488

Results for (top 100 genes) for ER-
Confusion matrix:
[[14  7]
 [ 4  7]]
AUC:                     0.81
Accuracy:                0.66
Sensitivity (Recall):0.64
Specificity:             0.67
PPV (Precision):         0.50
NPV:                     0.78
Balanced Accuracy:       0.65
```

```
Analyzing ER- group with tuning, without SMOTE

 Analysis for ERN
Amount of probes: 159
(0=RD, 1=pCR):
pCR_label
0    104
1     55
Name: count, dtype: int64

Train dataset:
pCR_label
0    83
1    44
Name: count, dtype: int64
Test dataset:
pCR_label
0    21
1    11
Name: count, dtype: int64
Tuning (324 combinantions, cv=4)
Tuning (f2): 100%                                    324/324 [06:00<00:00,  1.11it/s]

Best params:
colsample_bytree: 1.0
learning_rate: 0.2
max_depth: 3
min_child_weight: 1
n_estimators: 100
Best f2: 0.488

Results for (top 100 genes) for ER-
Confusion matrix:
[[14  7]
 [ 6  5]]
AUC:                     0.55
Accuracy:                0.59
Sensitivity (Recall):0.45
Specificity:             0.67
PPV (Precision):         0.42
NPV:                     0.70
Balanced Accuracy:       0.56
```

```python
def roc_pr_curves(results_dict, label_prefix):
    y_true = results_dict["y_true"]
    y_proba = results_dict["y_proba"]

    fpr, tpr, _ = roc_curve(y_true, y_proba)
    precision, recall, _ = precision_recall_curve(y_true, y_proba)

    return {
        "fpr": fpr, "tpr": tpr, "roc_auc": auc(fpr, tpr),
        "precision": precision, "recall": recall, "pr_auc": auc(recall, precisi
        "label": label_prefix
    }

roc_pr_er_neg = roc_pr_curves(results_er_negative_with_tune, "ER-")

#ROC Curve
plt.figure()
plt.plot(roc_pr_er_neg["fpr"], roc_pr_er_neg["tpr"], label=f"ER- (AUC = {roc_pr
plt.plot([0, 1], [0, 1], linestyle='--', color='grey')
plt.title("ROC Curve")
plt.xlabel("False Positive Rate")
plt.ylabel("True Positive Rate")
plt.legend()
plt.grid(True)
plt.show()

#P-R Curve
plt.figure()
plt.plot(roc_pr_er_neg["recall"], roc_pr_er_neg["precision"], label=f"ER- (AUC
plt.title("Precision-Recall Curve")
plt.xlabel("Recall")
plt.ylabel("Precision")
plt.legend()
plt.grid(True)
plt.show()
```

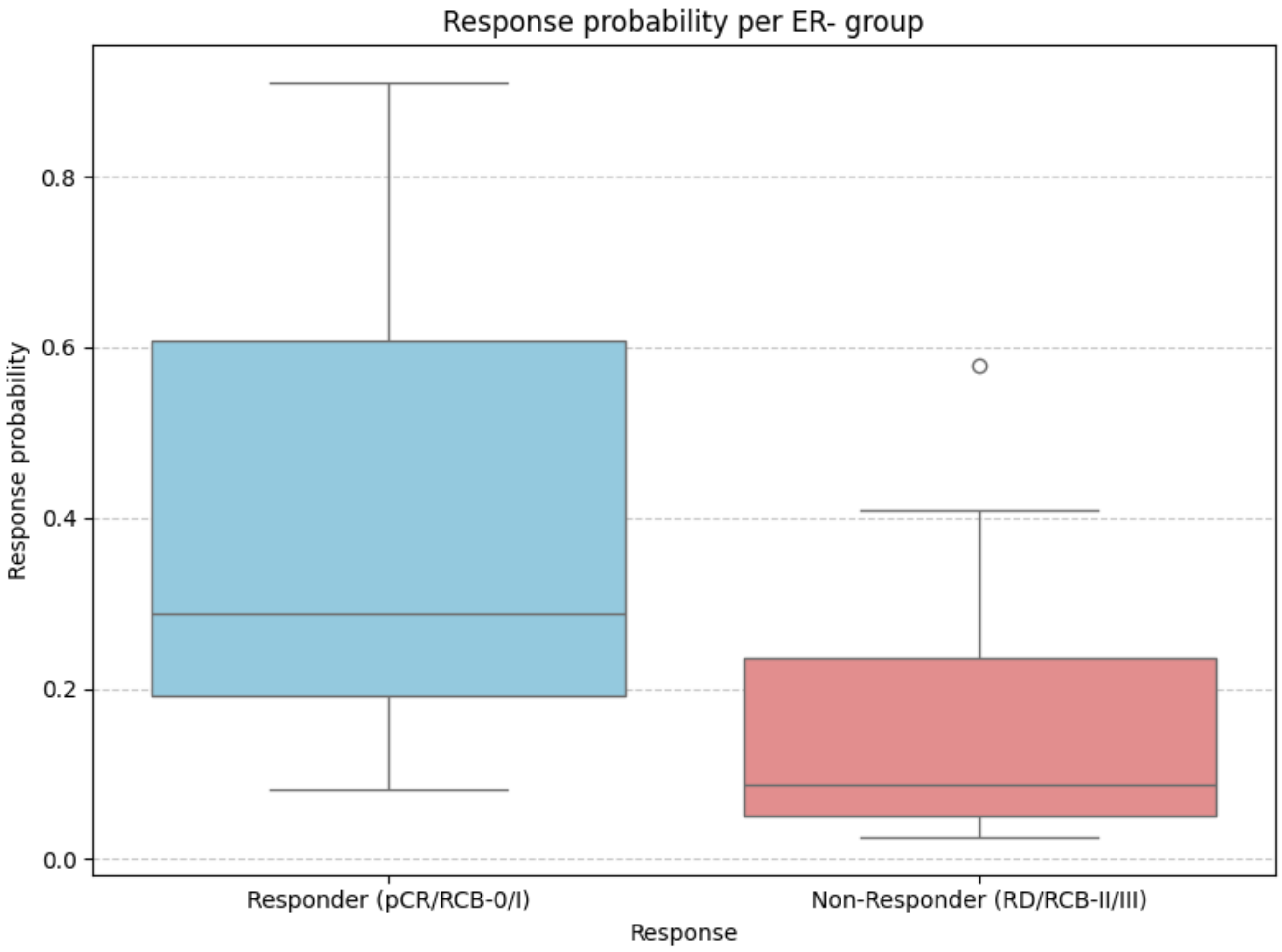

ROC Curve
ER− (AUC = 0.81)
True Positive Rate
False Positive Rate
0.0
0.2
0.4
0.6
0.8
1.0


Precision-Recall Curve
ER− (AUC = 0.73)
Precision
Recall
0.4
0.5
0.6
0.7
0.8
0.9
1.0
0.0
0.2
0.4
0.6
0.8
1.0

```
def probability_boxplots_ern(results_dict, title_suffix=""):

    y_true = results_dict["y_true"]
    y_proba = results_dict["y_proba"]

    boxplot_data = pd.DataFrame({
        'Response probability': y_proba,
        'Response': np.where(y_true == 1, 'Responder (pCR/RCB-0/I)', 'Non-Respo
    })

    plt.figure(figsize=(8, 6))
    sns.boxplot(x='Response', y='Response probability',
                data=boxplot_data,
                palette={'Responder (pCR/RCB-0/I)': 'skyblue', 'Non-Responder (
    plt.title(f'Response probability per {title_suffix} group')
    plt.xlabel('Response')
    plt.ylabel('Response probability')
    plt.grid(axis='y', linestyle='--', alpha=0.7)
    plt.tight_layout()

    plt.show()
```

```
probability_boxplots_ern(results_er_negative_with_tune, title_suffix="ER-")
```

```
/tmp/ipython-input-19-2460795971.py:12: FutureWarning:

Passing `palette` without assigning `hue` is deprecated and will be removed

  sns.boxplot(x='Response', y='Response probability',
```



```
#Finding the treshild
y_true = results_er_negative_with_tune["y_true"]
y_proba = results_er_negative_with_tune["y_proba"]

precision, recall, thresholds = precision_recall_curve(y_true, y_proba)

precision_trimmed = precision[:-1]
recall_trimmed = recall[:-1]

beta = 2
f2 = (1 + beta**2) * (precision_trimmed * recall_trimmed) / ((beta**2 * precisio

best_idx = np.argmax(f2)

#Metrisc
best_threshold = thresholds[best_idx]
best_recall = recall_trimmed[best_idx]
best_precision = precision_trimmed[best_idx]
best_f2 = f2[best_idx]

print(f"Best treshold for F2: {best_threshold:.3f}")
print(f"Recall: {best_recall:.3f}")
print(f"Precision: {best_precision:.3f}")
print(f"F2-score: {best_f2:.3f}")
```

```
Best treshold for F2: 0.081
Recall: 1.000
Precision: 0.500
F2-score: 0.833
```

ER+

```
def analyze_er_withgrid_1_for_erp(er_status_value, df_meta_final, df_expr_final
                           top_n_genes=100, threshold=0.05, test_size=0.2, cv=5

    #filtering data
    valid_labels = [ "RCB-0", "RCB-I", "RCB-0/I", "RCB-II", "RCB-III"]
    meta = df_meta_final[
        (df_meta_final["er_status_ihc"] == er_status_value) &
        (df_meta_final["pathologic_response_pcr_rd"].isin(valid_labels))
    ].copy()

    #0/1 label
    meta["pCR_label"] = meta["pathologic_response_pcr_rd"].isin([ "RCB-0", "RCE

    if verbose:
        print(f"\n Analysis for ER{er_status_value}")
        print(f"Amount of probes: {meta.shape[0]}")
        print(f"(0=RD, 1=pCR):\n{meta['pCR_label'].value_counts()}\n")
```

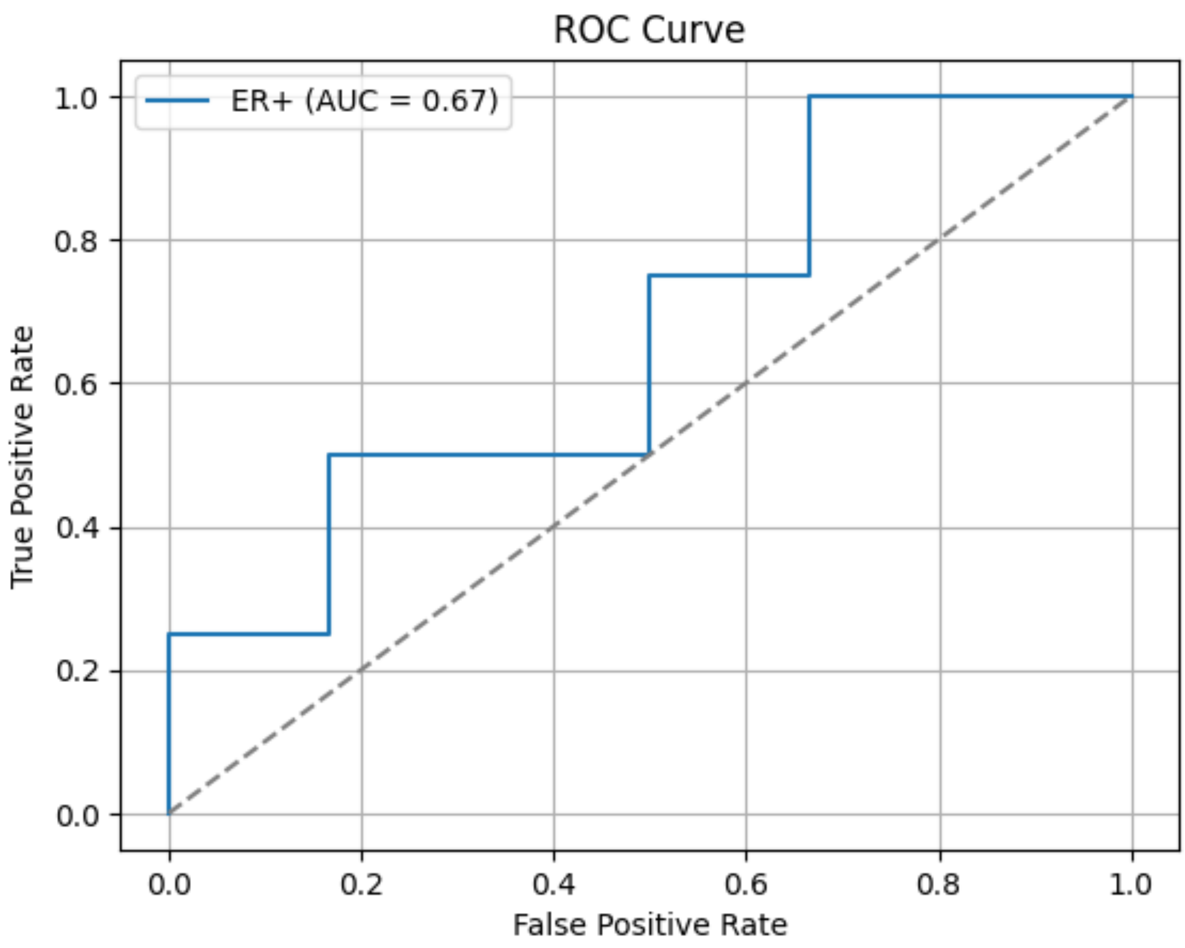
```
expr = df_expr_final[meta.index].T
y = meta["pCR_label"]

#Train and test data
train_indices, test_indices = train_test_split(
    meta.index,
    test_size=test_size,
    stratify=y,
    random_state=42
)

X_train_full = expr.loc[train_indices]
y_train_full = y.loc[train_indices]

X_test = expr.loc[test_indices]
y_test = y.loc[test_indices]

if verbose:
    print(f"Train dataset:")
    print(y_train_full.value_counts())
    print(f"Test dataset:")
    print(y_test.value_counts())

#Gene seleciton and training
selector = SelectKBest(mutual_info_classif, k=top_n_genes)
selector.fit(X_train_full, y_train_full)
top_genes = X_train_full.columns[selector.get_support()]

X_train = X_train_full[top_genes]
X_test = X_test[top_genes]

smote_sampler = SMOTE(random_state=42)

if use_tuning:
    best_params = tune_xgboost_hyperparams_withtqdm(X_train, y_train_full,
    xgb_model = XGBClassifier(
        tree_method="hist",
        device="cuda",
        eval_metric="logloss",
        random_state=42,
        **best_params
    )
else:
    xgb_model = XGBClassifier(
        tree_method="hist",
        device="cuda",
        eval_metric="logloss",
        random_state=42
    )
    model_pipeline = Pipeline([
        ('sampler', smote_sampler),
        ('classifier', xgb_model)
    ])

    model_pipeline.fit(X_train, y_train_full)
    y_proba_test = model_pipeline.predict_proba(X_test)[:, 1]
    y_pred_test = (y_proba_test >= threshold).astype(int)

    #Metrics
    cm = confusion_matrix(y_test, y_pred_test)
    tn, fp, fn, tp = cm.ravel()
    roc_auc = roc_auc_score(y_test, y_proba_test)
    acc = (tp + tn) / cm.sum()
    sens = tp / (tp + fn) if (tp + fn) > 0 else 0
    spec = tn / (tn + fp) if (tn + fp) > 0 else 0
    ppv = tp / (tp + fp) if (tp + fp) > 0 else 0
    npv = tn / (tn + fn) if (tn + fn) > 0 else 0
    bal_acc = (sens + spec) / 2

    if verbose:
        grupa = "ER+" if er_status_value == "P" else "ER-"
        print(f"\nResults for (top {top_n_genes} genes) for {grupa}")
        print("Confusion matrix:")
        print(cm)
        print(f"AUC:                 {roc_auc:.2f}")
        print(f"Accuracy:            {acc:.2f}")
        print(f"Sensitivity (Recall):{sens:.2f}")
        print(f"Specificity:         {spec:.2f}")
        print(f"PPV (Precision):     {ppv:.2f}")
        print(f"NPV:                 {npv:.2f}")
        print(f"Balanced Accuracy:   {bal_acc:.2f}")

    return {
        "group": "ER+" if er_status_value == "P" else "ER-",
        "top_genes": top_genes,
        "AUC": roc_auc,
        "Accuracy": acc,
        "Sensitivity": sens,
        "Specificity": spec,
        "PPV": ppv,
        "NPV": npv,
        "Balanced_Accuracy": bal_acc,
        "y_true": y_test,
        "y_proba": y_proba_test,
        "y":y
    }


print("Analyzing ER+ group with tuning")
results_er_positive_with_tune = analyze_er_withgrid_1_for_erp(
    er_status_value="P",
    df_meta_final=df_meta_final,
    df_expr_final=df_expr_final,
    top_n_genes=100,
    threshold=0.14,
    test_size=0.2,
    use_tuning=True,
    cv=4,
    verbose=True
)
```

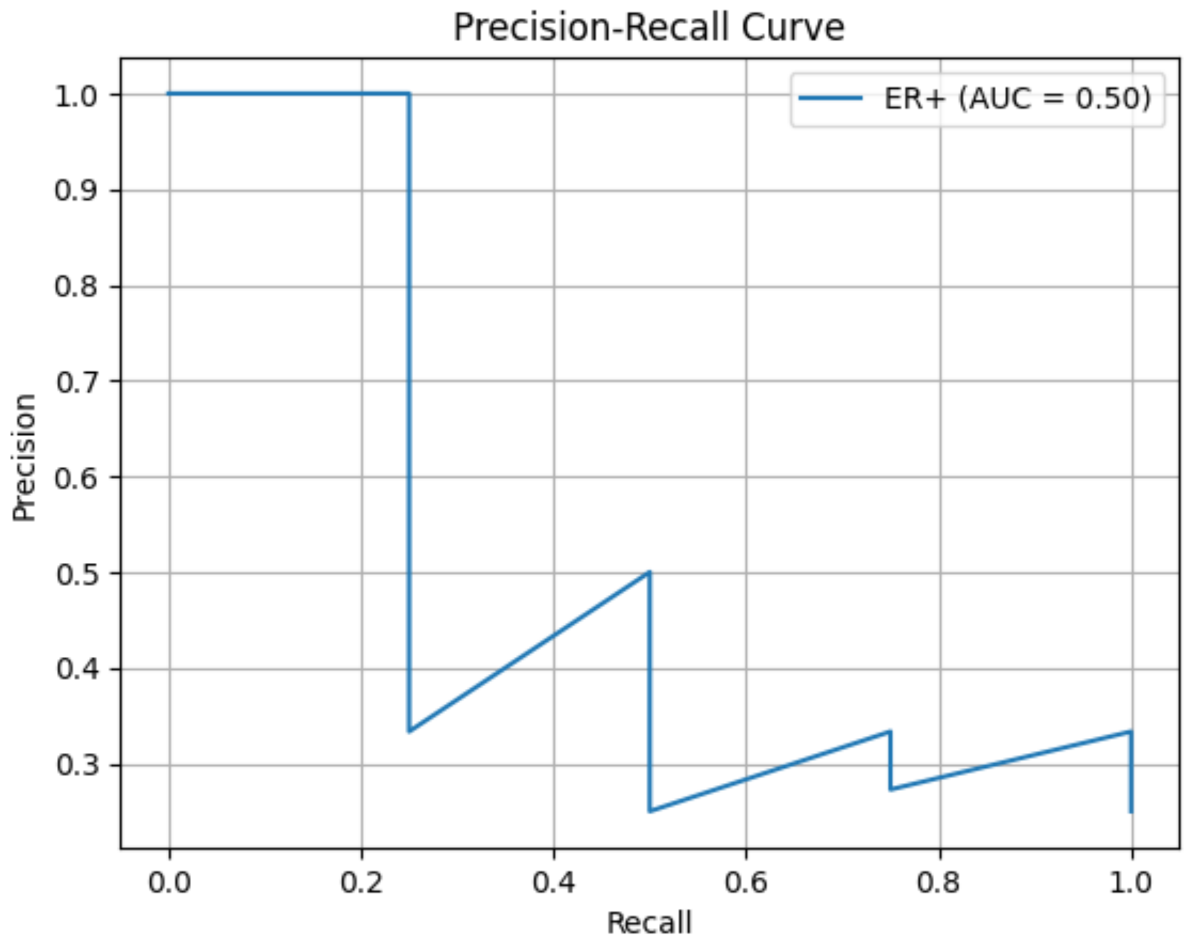
```
Analyzing ER+ group with tuning

 Analysis for ERP
Amount of probes: 79
(0=RD, 1=pCR):
pCR_label
0    61
1    18
Name: count, dtype: int64

Train dataset:
pCR_label
0    49
1    14
Name: count, dtype: int64
Test dataset:
pCR_label
0    12
1     4
Name: count, dtype: int64
Tuning (324 combinantions, cv=4)
Tuning (f2): 100%                                    324/324 [05:26<00:00,  1.21it/s]


Best params:
colsample_bytree: 0.6
learning_rate: 0.05
max_depth: 3
min_child_weight: 1
n_estimators: 200
Best f2: 0.463

Results for (top 100 genes) for ER+
Confusion matrix:
[[7 5]
 [2 2]]
AUC:                     0.67
Accuracy:                0.56
Sensitivity (Recall):0.50
Specificity:             0.58
PPV (Precision):         0.29
NPV:                     0.78
Balanced Accuracy:       0.54
```

```
def analyze_er_withgrid_1_for_erp_wirh_RD(er_status_value, df_meta_final, df_ex
                            top_n_genes=100, threshold=0.05, test_size=0.2, cv=5

    #filtering data
    valid_labels = ["pCR", "RCB-0", "RCB-I", "RD", "RCB-0/I", "RCB-II", "RCB-II
    meta = df_meta_final[
        (df_meta_final["er_status_ihc"] == er_status_value) &
        (df_meta_final["pathologic_response_pcr_rd"].isin(valid_labels))
    ].copy()
    #0/1 label
    meta["pCR_label"] = meta["pathologic_response_pcr_rd"].isin(["pCR", "RCB-0"

    if verbose:
        print(f"\n Analysis for ER{er_status_value}")
        print(f"Amount of probes: {meta.shape[0]}")
        print(f"(0=RD, 1=pCR):\n{meta['pCR_label'].value_counts()}\n")

    expr = df_expr_final[meta.index].T
    y = meta["pCR_label"]

    #Train and test data
    train_indices, test_indices = train_test_split(
        meta.index,
        test_size=test_size,
        stratify=y,
        random_state=42
    )

    X_train_full = expr.loc[train_indices]
    y_train_full = y.loc[train_indices]

    X_test = expr.loc[test_indices]
    y_test = y.loc[test_indices]

    if verbose:
        print(f"Train dataset:")
        print(y_train_full.value_counts())
        print(f"Test dataset:")
        print(y_test.value_counts())

    #Gene seleciton and training
    selector = SelectKBest(mutual_info_classif, k=top_n_genes)
    selector.fit(X_train_full, y_train_full)
    top_genes = X_train_full.columns[selector.get_support()]

    X_train = X_train_full[top_genes]
    X_test = X_test[top_genes]

    smote_sampler = SMOTE(random_state=42)

    if use_tuning:
        best_params = tune_xgboost_hyperparams_withtqdm(X_train, y_train_full,
        xgb_model = XGBClassifier(
            tree_method="hist",
            device="cuda",
            eval_metric="logloss",
            random_state=42,
            **best_params
        )
    else:
        xgb_model = XGBClassifier(
            tree_method="hist",
            device="cuda",
            eval_metric="logloss",
            random_state=42
        )

    model_pipeline = Pipeline([
        ('sampler', smote_sampler),
        ('classifier', xgb_model)
    ])

    model_pipeline.fit(X_train, y_train_full)
    y_proba_test = model_pipeline.predict_proba(X_test)[:, 1]
    y_pred_test = (y_proba_test >= threshold).astype(int)

    #Metrics
    cm = confusion_matrix(y_test, y_pred_test)
    tn, fp, fn, tp = cm.ravel()
    roc_auc = roc_auc_score(y_test, y_proba_test)
    acc = (tp + tn) / cm.sum()
    sens = tp / (tp + fn) if (tp + fn) > 0 else 0
    spec = tn / (tn + fp) if (tn + fp) > 0 else 0
    ppv = tp / (tp + fp) if (tp + fp) > 0 else 0
    npv = tn / (tn + fn) if (tn + fn) > 0 else 0
    bal_acc = (sens + spec) / 2

    if verbose:
        grupa = "ER+" if er_status_value == "P" else "ER-"
        print(f"\nResults for (top {top_n_genes} genes) for {grupa}")
        print("Confusion matrix:")
        print(cm)
        print(f"AUC:                 {roc_auc:.2f}")
        print(f"Accuracy:            {acc:.2f}")
        print(f"Sensitivity (Recall):{sens:.2f}")
        print(f"Specificity:         {spec:.2f}")
        print(f"PPV (Precision):     {ppv:.2f}")
        print(f"NPV:                 {npv:.2f}")
        print(f"Balanced Accuracy:   {bal_acc:.2f}")

    return {
        "group": "ER+" if er_status_value == "P" else "ER-",
        "top_genes": top_genes,
        "AUC": roc_auc,
        "Accuracy": acc,
        "Sensitivity": sens,
        "Specificity": spec,
        "PPV": ppv,
        "NPV": npv,
        "Balanced_Accuracy": bal_acc,
        "y_true": y_test,
        "y_proba": y_proba_test,
        "y":y
    }


print("Analyzing ER+ group with tuning and RD")
results_er_positive_with_tune_with_RD = analyze_er_withgrid_1_for_erp_wirh_RD(
    er_status_value="P",
    df_meta_final=df_meta_final,
    df_expr_final=df_expr_final,
    top_n_genes=100,
    threshold=0.14,
    test_size=0.2,
    use_tuning=True,
    cv=4,
    verbose=True
)
```

```
Analyzing ER+ group with tuning and RD

 Analysis for ERP
Amount of probes: 244
(0=RD, 1=pCR):
pCR_label
0    215
1     29
Name: count, dtype: int64

Train dataset:
pCR_label
0    172
1     23
Name: count, dtype: int64
Test dataset:
pCR_label
0    43
1     6
Name: count, dtype: int64
Tuning (324 combinantions, cv=4)
Tuning (f2): 100%                                   324/324 [05:43<00:00,  1.05it/s]

Best params:
colsample_bytree: 0.8
learning_rate: 0.05
max_depth: 3
min_child_weight: 1
n_estimators: 200
Best f2: 0.600

Results for (top 100 genes) for ER+
Confusion matrix:
[[35  8]
 [ 5  1]]
AUC:                     0.53
Accuracy:                0.73
Sensitivity (Recall):0.17
Specificity:             0.81
PPV (Precision):         0.11
NPV:                     0.88
Balanced Accuracy:       0.49
```

```python
def roc_pr_curves(results_dict, label_prefix):
    y_true = results_dict["y_true"]
    y_proba = results_dict["y_proba"]

    fpr, tpr, _ = roc_curve(y_true, y_proba)
    precision, recall, _ = precision_recall_curve(y_true, y_proba)

    return {
        "fpr": fpr, "tpr": tpr, "roc_auc": auc(fpr, tpr),
        "precision": precision, "recall": recall, "pr_auc": auc(recall, precisi
        "label": label_prefix
    }

roc_pr_er_pos = roc_pr_curves(results_er_positive_with_tune, "ER+")

#ROC Curve
plt.figure()
plt.plot(roc_pr_er_pos["fpr"], roc_pr_er_pos["tpr"], label=f"ER+ (AUC = {roc_pr
plt.plot([0, 1], [0, 1], linestyle='--', color='grey')
plt.title("ROC Curve")
plt.xlabel("False Positive Rate")
plt.ylabel("True Positive Rate")
plt.legend()
plt.grid(True)
plt.show()

#P-R Curve
plt.figure()
plt.plot(roc_pr_er_pos["recall"], roc_pr_er_pos["precision"], label=f"ER+ (AUC
plt.title("Precision-Recall Curve")
plt.xlabel("Recall")
plt.ylabel("Precision")
plt.legend()
plt.grid(True)
plt.show()
```


ROC Curve
ER+ (AUC = 0.67)
True Positive Rate
False Positive Rate
0.0
0.2
0.4
0.6
0.8
1.0


Precision-Recall Curve
ER+ (AUC = 0.50)
Precision
Recall
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
0.0
0.2
0.4
0.6
0.8
1.0

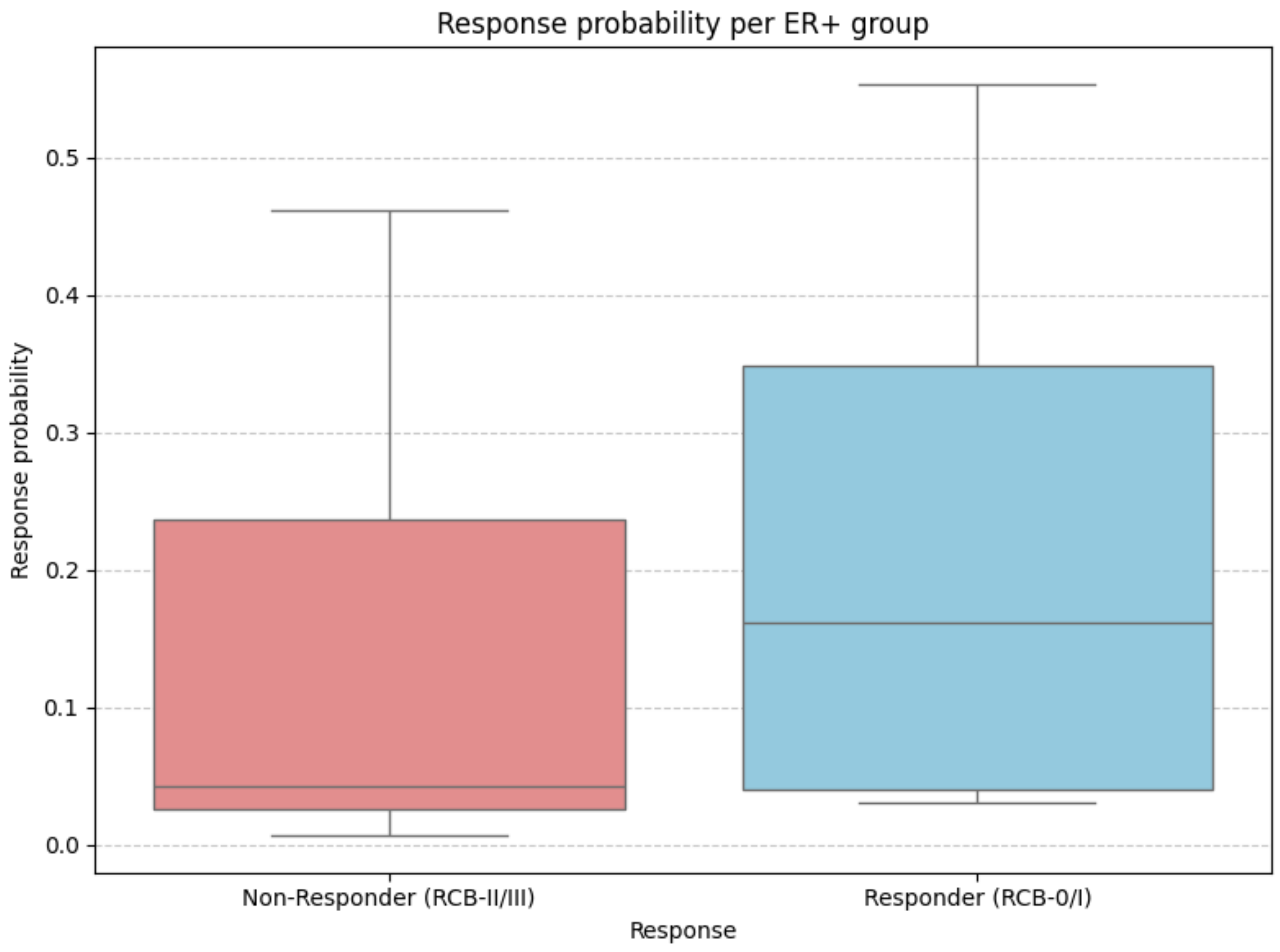
```
#Finding the treshild
y_true = results_er_positive_with_tune["y_true"]
y_proba = results_er_positive_with_tune["y_proba"]

precision, recall, thresholds = precision_recall_curve(y_true, y_proba)

precision_trimmed = precision[:-1]
recall_trimmed = recall[:-1]

beta = 2
f2 = (1 + beta**2) * (precision_trimmed * recall_trimmed) / ((beta**2 * precisi

best_idx = np.argmax(f2)

#Metrisc
best_threshold = thresholds[best_idx]
best_recall = recall_trimmed[best_idx]
best_precision = precision_trimmed[best_idx]
best_f2 = f2[best_idx]

print(f"Best treshold for F2: {best_threshold:.3f}")
print(f"Recall: {best_recall:.3f}")
print(f"Precision: {best_precision:.3f}")
print(f"F2-score: {best_f2:.3f}")
```

```
Best treshold for F2: 0.031
Recall: 1.000
Precision: 0.333
F2-score: 0.714
```

```
def probability_boxplots_erp(results_dict, title_suffix=""):

    y_true = results_dict["y_true"]
    y_proba = results_dict["y_proba"]

    boxplot_data = pd.DataFrame({
        'Response probability': y_proba,
        'Response': np.where(y_true == 1, 'Responder (RCB-0/I)', 'Non-Responder
    })

    plt.figure(figsize=(8, 6))
    sns.boxplot(x='Response', y='Response probability',
                data=boxplot_data,
                palette={'Responder (RCB-0/I)': 'skyblue', 'Non-Responder (RCB-
    plt.title(f'Response probability per {title_suffix} group')
    plt.xlabel('Response')
    plt.ylabel('Response probability')
    plt.grid(axis='y', linestyle='--', alpha=0.7)
    plt.tight_layout()

    plt.show()
```

```
probability_boxplots_erp(results_er_positive_with_tune, title_suffix="ER+")
```

```
/tmp/ipython-input-23-3286981609.py:12: FutureWarning:

Passing `palette` without assigning `hue` is deprecated and will be removed

  sns.boxplot(x='Response', y='Response probability',
```

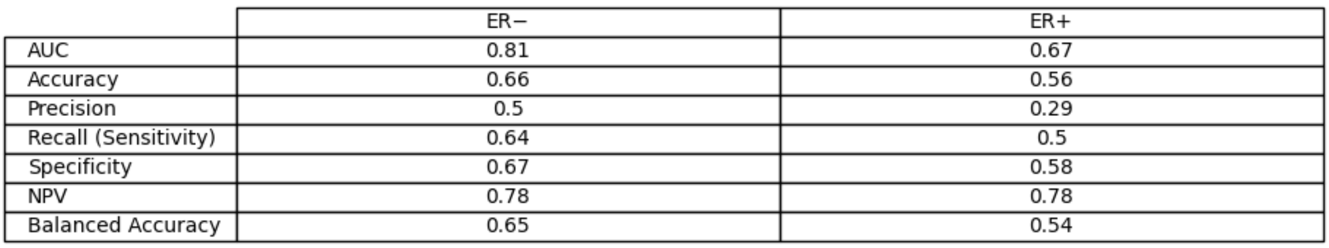


```python
results_list = [results_er_negative_with_tune, results_er_positive_with_tune]

metrics_df = pd.DataFrame({
    r["group"]: {
        "AUC": r["AUC"],
        "Accuracy": r["Accuracy"],
        "Precision": r["PPV"],
        "Recall (Sensitivity)": r["Sensitivity"],
        "Specificity": r["Specificity"],
        "NPV": r["NPV"],
        "Balanced Accuracy": r["Balanced_Accuracy"]
    }
    for r in results_list
})

metrics_df
```

	ER−	ER+
AUC	0.805195	0.666667
Accuracy	0.656250	0.562500
Precision	0.500000	0.285714
Recall (Sensitivity)	0.636364	0.500000
Specificity	0.666667	0.583333
NPV	0.777778	0.777778
Balanced Accuracy	0.651515	0.541667

Next steps: Generate code with `metrics_df` View recommended plots New interactive sheet

```
fig, ax = plt.subplots(figsize=(8, 4))
ax.axis('off')

table = ax.table(
    cellText=metrics_df.round(2).values,
    rowLabels=metrics_df.index,
    colLabels=metrics_df.columns,
    cellLoc='center',
    loc='center'
)

table.auto_set_font_size(False)
table.set_fontsize(10)
table.scale(1.2, 1.2)

plt.savefig("metrics_table_XGBOOST.png", bbox_inches='tight', dpi=300)
```



	ER−	ER+
AUC	0.81	0.67
Accuracy	0.66	0.56
Precision	0.5	0.29
Recall (Sensitivity)	0.64	0.5
Specificity	0.67	0.58
NPV	0.78	0.78
Balanced Accuracy	0.65	0.54

```
# Analyzing genes
genes_pos = set(results_er_positive_with_tune["top_genes"])
genes_neg = set(results_er_negative_with_tune["top_genes"])

common_genes = genes_pos & genes_neg
unique_pos = genes_pos - genes_neg
unique_neg = genes_neg - genes_pos

max_len = max(len(common_genes), len(unique_pos), len(unique_neg))

def pad_list(l, n):
    return list(l) + [None]*(n - len(l))

gene_df = pd.DataFrame({
    "Common": pad_list(common_genes, max_len),
    "Unique ER+": pad_list(unique_pos, max_len),
    "Unique ER-": pad_list(unique_neg, max_len)
})

gene_df.head(10)
```

	Common	Unique ER+	Unique ER-
0	None	31807_at	207226_at
1	None	211363_s_at	221122_at
2	None	210247_at	220377_at
3	None	202819_s_at	202439_s_at
4	None	203181_x_at	211131_s_at
5	None	214083_at	222225_at
6	None	211250_s_at	216875_x_at
7	None	218757_s_at	216892_at
8	None	207996_s_at	206818_s_at
9	None	208329_at	219442_at

```
probes = gene_df[gene_df['Common'].notna()]['Common'].tolist()
```

https://www.thermofisher.com/pl/en/home/life-science/microarray-analysis/microarray-data-analysis/genechip-array-annotation-files.html

```
annotation_file = pd.read_csv('/content/drive/MyDrive/modelowanie/projekt/HG-U13
annotation_file.head()
```

	Probe Set ID	GeneChip Array	Species Scientific Name	Annotation Date	Sequence Type	Sequence Source	Tra ID(Array I
0	1007_s_at	Human Genome U133A Array	Homo sapiens	Mar 30, 2016	Exemplar sequence	Affymetrix Proprietary Database	U487
1	1053_at	Human Genome U133A Array	Homo sapiens	Mar 30, 2016	Exemplar sequence	GenBank	
2	117_at	Human Genome U133A Array	Homo sapiens	Mar 30, 2016	Exemplar sequence	Affymetrix Proprietary Database	X5
3	121_at	Human Genome U133A Array	Homo sapiens	Mar 30, 2016	Exemplar sequence	GenBank	
4	1255_g_at	Human Genome U133A Array	Homo sapiens	Mar 30, 2016	Exemplar sequence	Affymetrix Proprietary Database	L36861expar

5 rows × 41 columns

```
gene_info = annotation_file[annotation_file['Probe Set ID'].isin(probes)]

print(gene_info[['Probe Set ID', 'Gene Symbol', 'Gene Title']])
```

```
Empty DataFrame
Columns: [Probe Set ID, Gene Symbol, Gene Title]
Index: []
```